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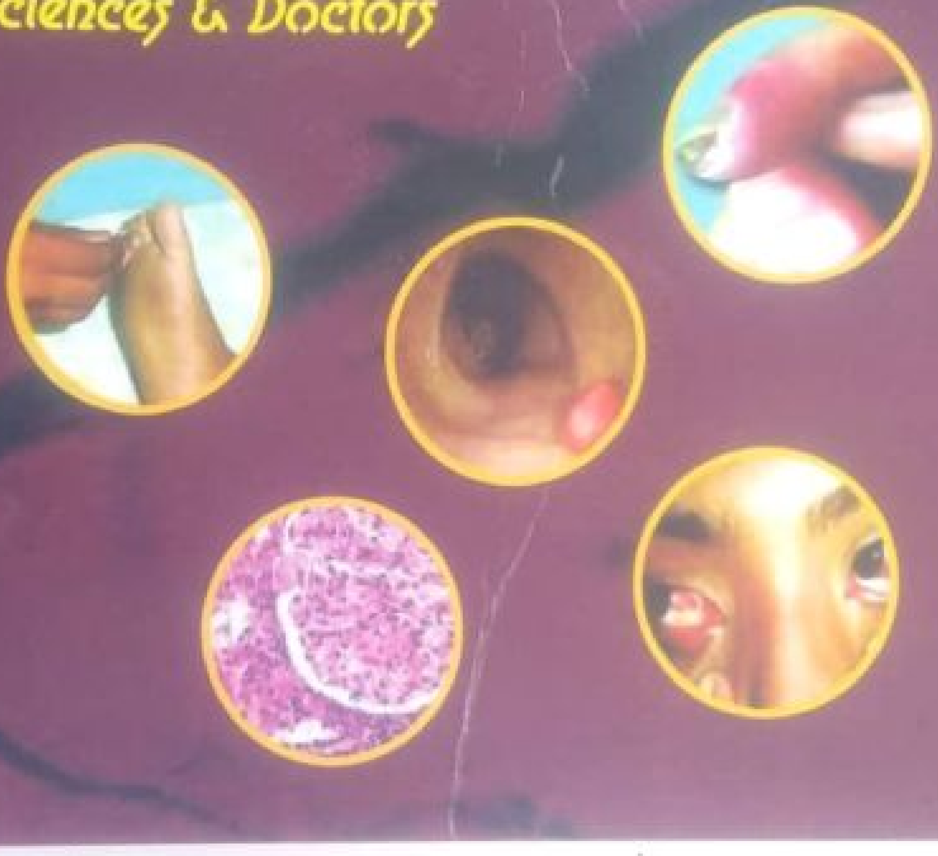
MEDICAL EDUCATION

Review of Medicine in Seconds

For MBBS, BDS, DPT, MIT, MLT, Pharm-D, Allied Health Sciences & Doctors



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Review of the Medicine in Seconds

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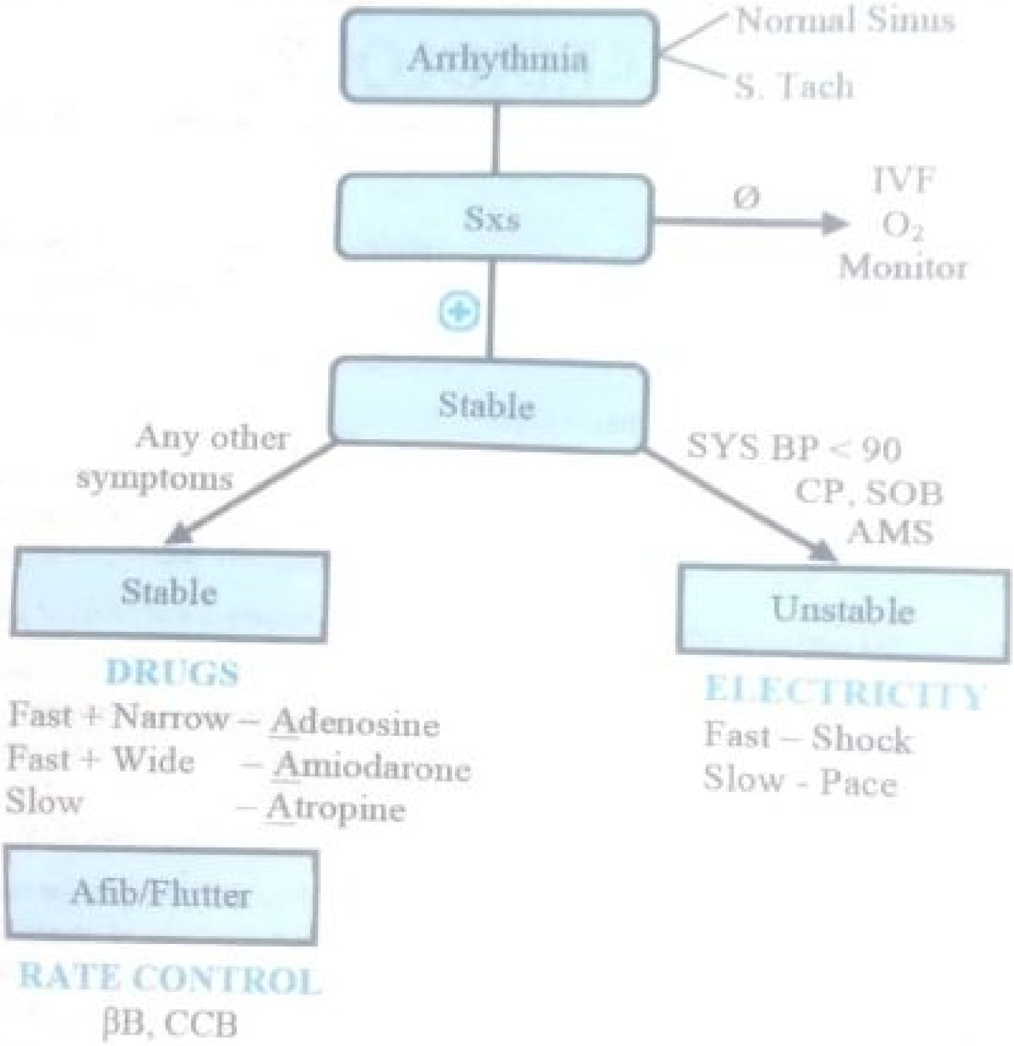

Arrhythmia
Normal Sinus
S. Tach
Sxs
Ø
IVF
O2
Monitor
⊕
Stable
Any other symptoms
SYS BP < 90
CP, SOB
AMS
Stable
Unstable
DRUGS
Fast + Narrow – Adenosine
Fast + Wide – Amiodarone
Slow – Atropine
ELECTRICITY
Fast – Shock
Slow - Pace
Afib/Flutter
RATE CONTROL
βB, CCB

Tachy Rhythms

- Sinus Tachycardia
- Supraventricular Tachycardia
- Multifocal Atrial Tachycardia
- Afib
- Aflutter

Atrial
Narrow

- Vtach
- Vfib
- Torsades

Ventricular
Wide

Brady Rhythms

- Sinus Bradycardia
- 1^o Block
- 2^o Block
- 3^o Block

Varying degree
of PR intervals

- Junctional
- Idioventricular

Intervention	*Heart Rate*	*QRS Complex*	*Stability*
Pacer	Brady	Any	Unstable
Cardioversion	Tachy	Any	Unstable
Atropine	Brady	Any	Stable
Adenosine	Tachy	Narrow	Stable
Amiodarone	Tachy	Wide	Stable
Rate Control	Tachy	Afib/Flutter	Stable

"Rate Control" = Verapamil / Diltiazem, Metoprolol

- If you've chosen **stable/electricity** it's a slightly more difficult task. For **stable rhythms, there are three, maybe four, options.**
- 1 - If the rhythm is **fast + narrow + stable** use **adenosine.**
- 2 - If the rhythm's **fast + wide + stable** use **amiodarone.**
- 3 - If the rhythm's **slow + stable** use **atropine (epi drips can also be used in the new ACLS roll out).**
- 4 - If the rhythm's **Afib/Aflutter** (note this is the only rhythm that actually had to be identified to do the right intervention), **rate control** is preferred.
- If they were **unstable shock** them since afib usually presents as a tachycardia. By "rate control" we mean **Beta Blockers** or **Calcium Channel Blockers.**

RHYTHMS

Supraventricular tachycardia is an **aberrant reentry** that bypasses the SA node. It's **narrow** (atrial), **fast** (tachycardia), and will be distinguished from a sinus tachycardia by a **resting heart rate > 150** + the loss of **p-waves** (can you tell p-waves from t-waves?). It responds to **adenosine.**

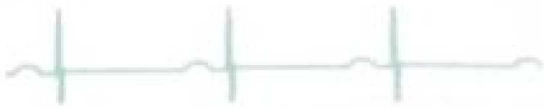
Ventricular Tachycardia is a **wide complex** and **regular** tachycardia. Look for the **"tombstones."** Since it's ventricular there are **no paves** at all - just the **QRS complexes.** It responds to **amiodarone (newer/better)** or **lidocaine (older/cheaper).**

Atrial Fibrillation can be identified by a **narrow complex** tachycardia with a **chaotic background, absent p-waves,** and an **irregularly irregular** R-R interval. It has a special treatment algorithm.

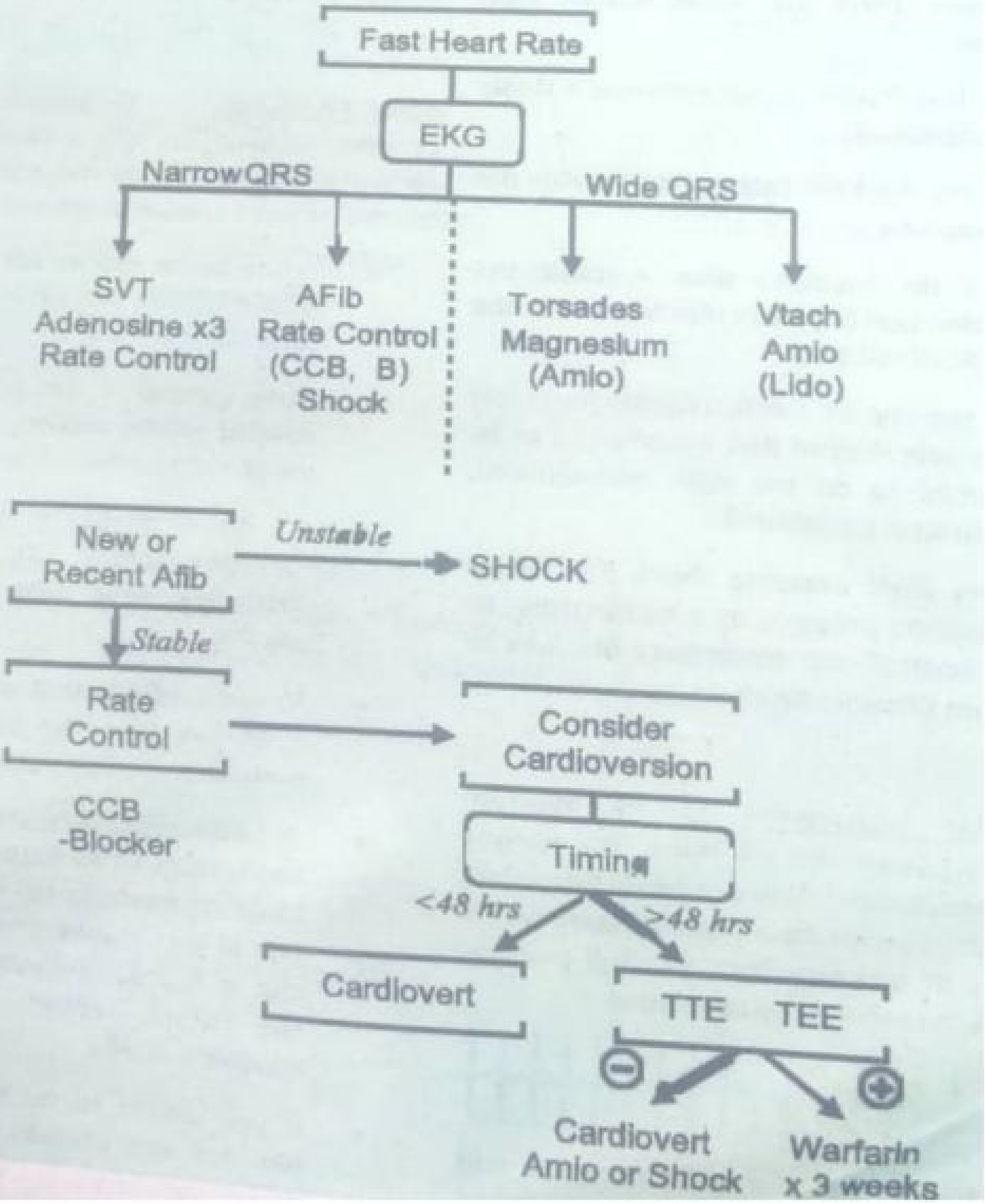
- In the **acute setting (ACLS in a nutshell)** simply decide between **shock** and **rate control.**
- **Rate control** is just as good as **rhythm control (cardioversion).** But, you have to weigh risks and benefits in each patient.
- If the goal is **rhythm control (cardioversion).** It's necessary to determine **how long** the Afib's been present.
- Simply **cardioverting an Afib** that's **lasted > 48 hrs** runs the risk of throwing an **embolism** (and a stroke).
- If **< 48hours cardioversion** is ok. But if it's been present **> 48 hours** the patient needs to go on **warfarin** for **four weeks.** At the **end of four weeks,** the **TEE** is done. If **no clot is found,** cardioversion is done and the patient remains on warfarin for another 4 weeks.
- If you decide to do **rate control (beta blockers and calcium channel blockers) anticoagulation** may still be needed.

- Decide this using the **CHADS2 score**. The higher the score the higher the risk of embolism and the more likely the patient is to benefit from **warfarin (2+ CHADS2)**.
- Now, the **Xa- or Thrombin-inhibitors** can be used **instead (1+ CHADS2). Examples** include **apixiban** or **dabigatran**.

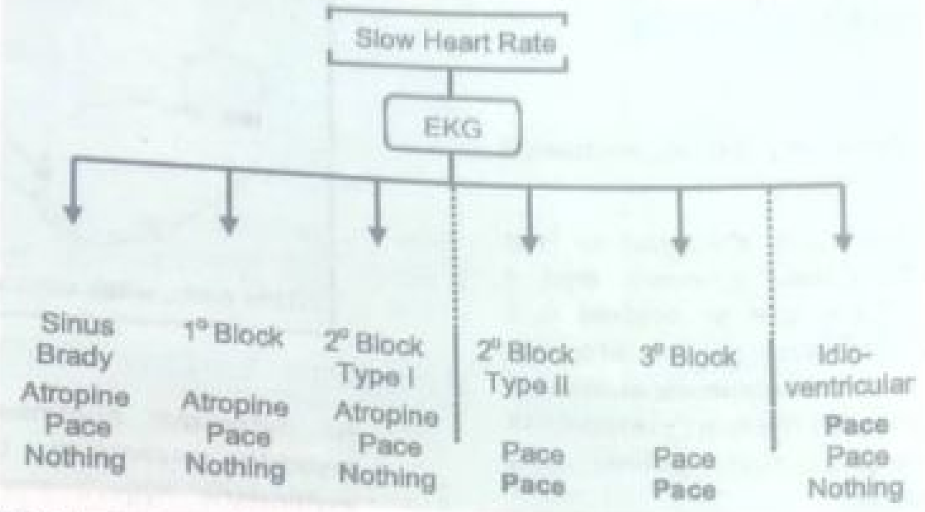
Sinus bradycardia is simply a slow normal sinus rhythm. The blocks are a worsening of that normal bradycardia. Almost everything responds to **Atropine** until it gets really bad - then **only pacing will do.**



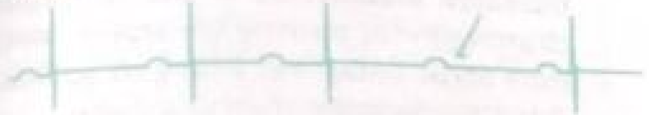
1° AV Block is characterized by **prolonged PR interval**. There's no interval between **beats, but** each There are no dropped beats.



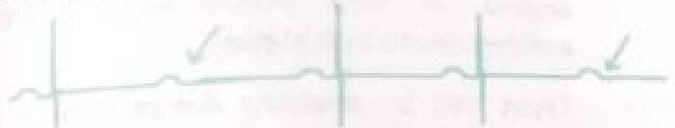
Fast Heart Rate
EKG
NarrowQRS
Wide QRS
SVT
Adenosine x3
Rate Control
AFib
Rate Control
(CCB, B)
Shock
Torsades
Magnesium
(Amio)
Vtach
Amio
(Lido)
New or
Recent Afib
Unstable
SHOCK
Stable
Rate
Control
CCB
-Blocker
Consider
Cardioversion
Timing
<48 hrs
>48 hrs
Cardiovert
TTE TEE
Cardiovert
Amio or Shock
Warfarin
x 3 weeks


Slow Heart Rate
EKG
Sinus Brady
Atropine
Pace
Nothing
1° Block
Atropine
Pace
Nothing
2° Block Type I
Atropine
Pace
Nothing
2° Block Type II
Pace
Pace
3° Block
Pace
Pace
Idio-ventricular
Pace
Pace
Nothing

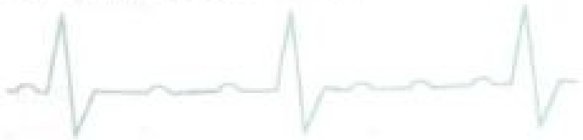
2° AV Block Type I is a **normal rhythm** with a constantly **prolonging PR interval** with **each beat**, until a QRS complex is **finally dropped**. The signal comes from the atria so there is a **narrow QRS complex**.



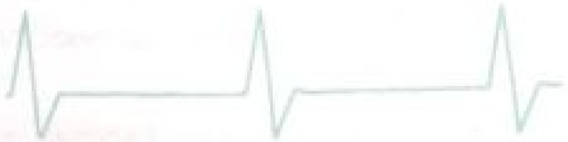
2o AV Block Type II has a **normal PR interval** but simply **drops QRSs** randomly. The **signal** comes from the **atria so the QRS complexes are narrow.** This is the **most severe** a rhythm can be **before atropine no longer works.**



3° AV Block. There's total **AV node dissociation.** The **Ps march out (regular interval between P waves)** and the **QRSs march out (regular interval between QRS complexes).** At times, the **P waves** may seem **lost or dropped**; the **QRS complex** occurs at the same time and obscures the p wave. Because the **impulse** comes from the **ventricles it's a wide QRS complex**. In general, **avoid atropine** (just pace). This is controversial.



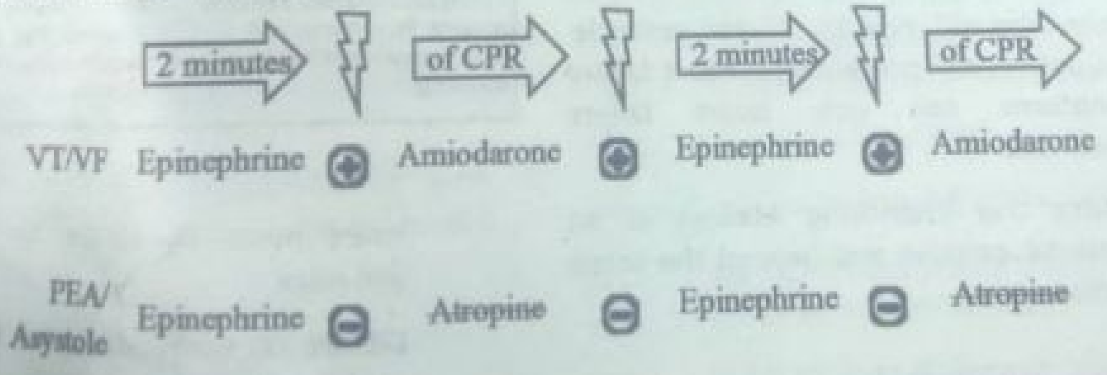
Idioventricular Rhythm is a rhythm without atrial activity. Only the ventricles are contracting, only the ventricles have electrical activity. It looks like a 3° block, but **without p waves. Avoid atropine** (it **won't work),** as there is no atrial conduction at all, so **just pace.**



This is not every rhythm you could see. **You'll see a rhythm, MAYBE two on the test. MAYBE.**

CARDIAC ARREST

When dead, remember 1 thing: compressions. Everything is based around 2 minutes of CPR. 2 minutes of CPR, check a pulse, check a rhythm, shock if indicated. Shock is indicated only in Vtach/Vfib arrest. Always start with Epi. Only in VT/VF can you shock, and so too only in VT/VF can antiarrhythmics be used. That's it. This is almost never tested on Step 2 but is here completeness.


2 minutes
of CPR
2 minutes
of CPR
VT/VF
Epinephrine
Amiodarone
Epinephrine
Amiodarone
PEA/ Asystole
Epinephrine
Atropine
Epinephrine
Atropine

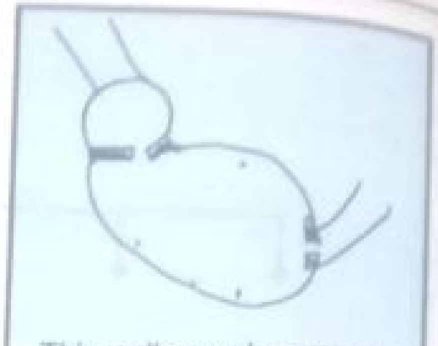
CARDIOMYOPATHY

Introduction

- There are **three very** distinct **mechanical diseases** of the heart.
- Anything that causes the heart to **"not work right" (cardio = heart, myo = muscle, pathy = bad or broken)** is a cardiomyopathy. Whether it's **Afib, MI, infection, toxins, autoimmune disease** - it doesn't matter. It's the heart's response to these stressors that defines the cardiomyopathy.

1) Dilated Cardiomyopathy

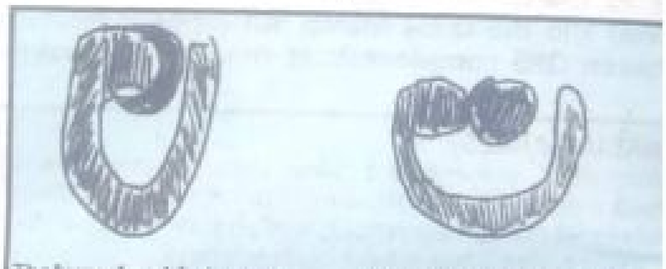
- The heart works by **overlying actin and myosin filaments**.
- If they start **too close together** there's nowhere for them to contract.
- Conversely, if they start too far apart there's no overlap to generate contraction.
- When the heart **dilates** the wall gets **stretched out** (so it's thin) and has a **decreased contractility** (producing a **systolic heart failure**).
- The heart becomes a bag of blood rather than a pump.
- The etiologies are vast: **ischemia**, **valve disease**, **idiopathic**, **infectious**, **metabolic**, **alcoholic**, **autoimmune**, etc.
- The point is that diagnosis and management are the same, regardless of the etiologies.
- A **Chest X-ray** will show an enlarged heart, while **Echo** will show the **dilated ventricle**. The patient will present with **heart failure symptoms** and gets **heart failure treatment**.
- Getting the underlying etiology is an academic exercise and beyond the scope of this course.



Thin walls, weak contraction

2) Hypertrophic Cardiomyopathy (HCM)

- An **autosomal dominant** mutatio **myocyte sarcomeres**, this causes **asymmetric hypertrophy** of the s wall. Since it occludes the **aortic outl** presents just like an **aortic stenosis** ex that it's heard at the **apex** and **impro with increased preload**. **Why?** Bec **increased preload** causes the ventric chamber to fill, pushing the septum a from aortic outlet and letting blood fl This is the opposite of aortic stenosis.
- Also, HCM is found in **young people** w AS is found in the **elderly**.
- Symptoms may be **SOB (most comm angina**, or what people know it **sudden death in athletes**.
- **Treat** this by **avoiding dehydration** a with **1~-Blockers** to allow an increase ventricular filling.



The **hypertrophied septum** growing from the **normal septum overrides the aortic opening**

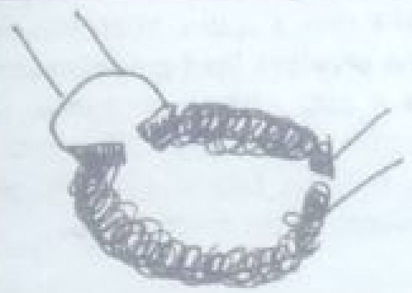
By increasing preload the chamber fills, pushing the septum away from the aortic opening

2) Restrictive Cardiomyopathy

- Heart muscle should be able to contr and relax.
- **Dilated cardiomyopathy** has trouble with contractility - getting the **blood OUT**

(systolic failure).

- **Restrictive cardiomyopathy** has trouble relaxing - getting **blood in (diastolic failure).** It can't relax to accept blood because there's **" junk in the way."**
- It's caused by **Sarcoid**, **amyloid**, **hemochromatosis, cancer,** and **fibrosis** as well as other causes that are **really rare.**
- **Treatment is tricky** – it's necessary to maintain an adequate preload while not overloading the **pulmonary vasculature.**
- **Gentle diuresis** and **heart rate control** are essential. **Transplant** in refractory cases.

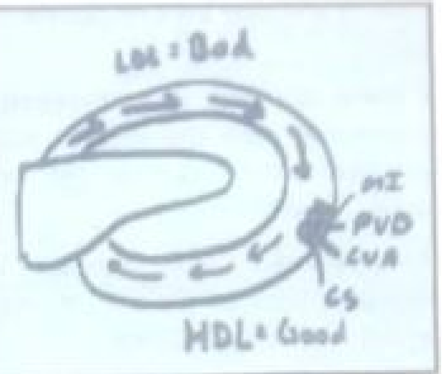


All the junk in the myocardium won't let the heart relax!!!

HYPERCHOLESTEREMIA

Cholesterol

- Cholesterol is needed for cells to exist.
- The problem is that too much cholesterol leads to the development of plaques, the things that cause **atherosclerosis.**
- There is **bad cholesterol (LDL)** that is responsible for bringing the **cholesterol to the periphery.** Too much of it makes plaques form.
- The **good cholesterol (HDL) clears those plaques** and brings the **cholesterol back to the liver** for processing.
- It makes sense that we' d want to **decrease the LDL** and **increase the HDL.**
- Turns [illegible] that's not true.
- The goal is to [illegible] people on a statin.



Why Statins?

Although controversial, **the most recent lipid guidelines** have said that targeting a specific number did not improve outcomes. What improved outcomes **(stroke, heart attack, and death)** was to be on a **high-intensity statin. It's empiric.**

Who Gets a Statin?

There are **four groups** of people who should be on a **high-intensity statin (atorvastatin or rosuvastatin).**

^{1} Anyone with any vascular disease **(stroke, coronary artery disease, peripheral vascular disease,** or **carotid stenosis)** or ^{2} **LDL > 190.** If a patient has **vascular disease or an LDL > 190,** regardless of anything else, they're on a statin. It gets a bit trickier when one of these two criteria isn't present.

If the patient has an **LDL < 70** they do **NOT need a statin. Vascular disease and LDL > 190** trump this statement, though the intensity will likely be decreased.

So groups ^{3} **Diabetes and** ^{4}**Calculated risk** go something like this. If the patient has an **LDL 70-189** AND are **Age 40-75** AND are **either a diabetic or have a 10-year calculated risk, they get a statin.** That **10-year calculated risk thing just means "do you have 2 or more vascular risk factors"** but in a more convoluted way you shouldn't memorize.

What Statin Should You Give?

The goal is to be on **high-intensity statin.**

- Start a moderate-intensity and increase the dose to high-intensity.
- If there's **liver disease** or **renal disease,**

start at and stay on a moderate-intensity statin.

- If there are signs of **statin-toxicity** during treatment, **stop the statin** until the signs go away. Then **restart the statin at a lower dose.**
- **Anaphylaxis** would be an exception, though the incidence is so low it essentially doesn't count.

Evaluation of Statins – What and When?

- **Baseline** values of **Lipids, A1 c, CK,** and **LFTs** are required before starting a statin.
- You want to know what their baselines are to allow comparison if something happens.
- **Lipids** are assessed **annually** (NOT q3months).
- **CK** and **LFTs** are **NOT** checked routinely. Assess them only when there's **evidence of disease.**
- **Myositis** presents with **soreness, weakness, or muscle pain.**
- **Hepatitis** presents with **right upper quadrant abdominal pain or jaundice.**

hen it is an option, the right answer is always:

1. *Lifestyle = Diet / Exercise*
2. *Adherence = Medication and Lifestyle*

o Needs a Statin?

1. *Vascular Disease = MI, CVA, PVD, CS*
2. *LDL > 190*
3. *LDL 70-189 + Age*
   + Diabetes

. *LDL 70-189 + Age*
   + Calculated Risk = "Risk Factors"

tors for Coronary Artery Disease

Diabetes
Smoking
Hypertension
yslipidemia
ge > 55 for women, > 45 for men

High-Intensity	Moderate-Intensity	Low-Intensity
Atorva 40, 80	**Atorva 10,20**	______
Rosuva 20, 40	**Rosuva 5,10**	______
______	Simvastatin 20,40	Simvastatin 5,10
______	Pravastatin 40, 80	Pravastatin 10,2
______	Lovastatin 40	Lova 20

Monitoring Statin Therapy

Baseline	**Routine**	**Symptoms**
Lipids	q1y	______
A1c	DM = q3mo	______
CK	______	Muscle Sxs
LFTs	______	Hepatitis

Statin-Myositis Stop Statin… Start a lower dose
Statin-Hepatitis Stop Statin… Restart at a lower do

The way the test will go after your knowledge of other lipid medications (which is still viable test fodder) is by giving a patient who, for whatever reason, **CAN'T** take a statin. Then the **door opens to follow the previous lipid guidelines of reducing the LDL to < 100** with medications. Of course, lifestyle modifications and adherence become paramount, but the test is going to get you to answer questions about medications.

Some highlights:

- **Fibrates** are the **second line** to statins. They have the same side effect profile but are also really good at getting the LDL down and the HDL up. They make sense.
- **Niacin** is a board favorite because it causes flushing. While Niacin has not been shown to have mortality benefit, it makes for a great test question. Treat the flushing **with Aspirin** prophylaxis.
- **Bile Acid resins** and **Ezetimibe** block absorption of fatty-related stuff. That leads to a fatty stool. Fatty stool causes osmotic diarrhea.

Drug	*Effect*	*Mechanism*	*Side Effect*
Statins	↓LDL ↓TG	HMG-CoA reductase	**Myositis** **LFT ↑**
Fibrates	↓TC ↑HDL	Lipoprotein Lipase	**Myositis** **LFT ↑**
Ezetimibe	↓LDL	Cholesterol Absorption	**Diarrhea**
Niacin	↑HDL ↓LDL	↓ Fatty Acid Release ↓ LDL Synthesis	**Flushing (treat with ASA)**
Bile Acid Resins	↓LDL	Bile Acid Reabsorption	**Diarrhea**

MYOCARDIAL ISCHEMIA

Introduction:

- **Coronary artery disease** is blockage in the heart arteries.
- It's caused by **chronically progressive atherosclerosis** (the **plaque**) that obstructs the lumen, decreasing the ability of the arteries to perfuse the myocardium.
- This produces ischemia when cardiac demand increases; there's an imbalance in the demand to supply ratio.
- For these conditions, both **reperfusion (getting rid of the plaque) and reducing the workload** of the heart will improve symptoms.
- When an **acute thrombus** forms from **endothelial injury the lumen** can quickly become occluded, resulting in a **supply ischemia**; no amount of demand reduction will save this tissue.
- **Reperfusion** is required to prevent myocardial death.
- The spectrum of coronary artery disease begins with **stable angina** where the coronary artery disease is known and the patient knows how far they can go before symptoms start.
- **Unstable angina** is worsening of symptoms with less work, more pain with the same work, or pain refractory to nitroglycerin.
- **NSTEMI** is still demand ischemia, but there's elevation of the troponins.
- **STEMI** implies acute thrombosis and transmural infarct.

isk Factors

- CAD is just vascular disease in the heart **arteries**; the risk factors are the same for all **vascular** disease.
- **Diabetes**, [illegible]**king**, **Hypertension**, **Dyslipidemia**, and [illegible]**sity** are **modifiable** risk factors.
- **Age (M > 45, F> 55)** and **family history** of early vascular disease are **non-modifiable** risk factors.

	Stable Angina	*Unstable Angina*	*NSTEMI*	*STEMI*
Pain	Exercise	@ rest	@ rest	@ rest
Relief	Rest + Nitrates	∅	∅	∅
Biomarkers	∅	∅	↑	↑
ST Δs	∅	∅	∅	↑
Pathology	70%	90%	90%	100%

Sxs	*Assoc Sxs*	*Risk Factors*
1. Substernal	Dyspnea	Diabetes
2. Exertional	N/V	Smoking
3. Relieved with NTG	Presyncope	HTN
		HLD
3/3 = Typical		Family Hx
2/3 = Atypical		Age > 45 M > 55 F
0-1 = Nonanginal		

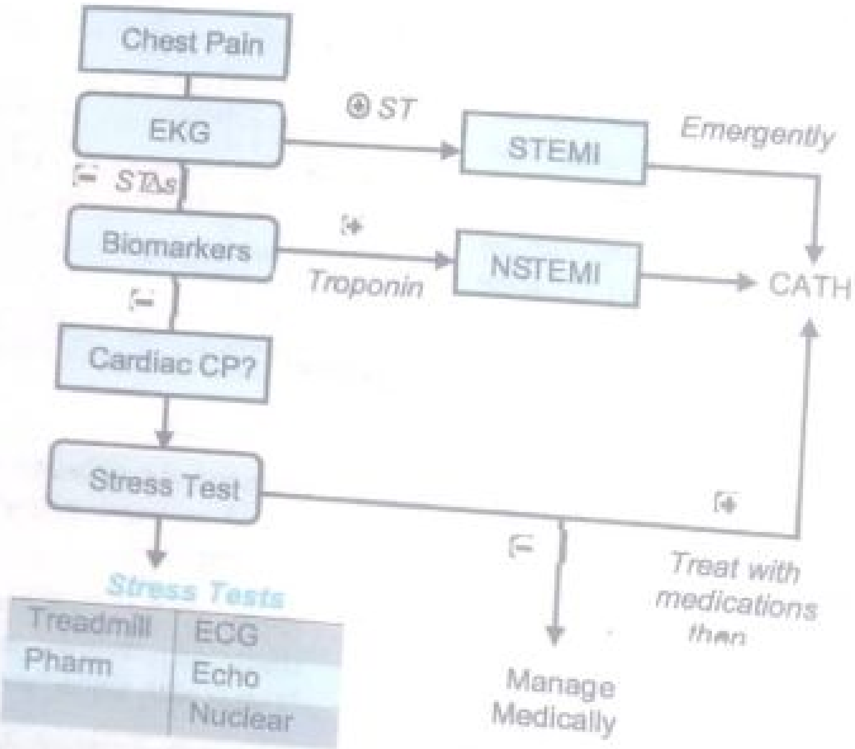
Patient Presentation

- **Diamond classification** identifies patients' risk of coronary artery disease based on the symptoms.
- There are **three components.** ^{1}**Substernal** chest pain,^{2}**Worse with** Exertion, and ^{3}**Better with Nitroglycerin**.
- **3/3** is called **typical, 2/3** is called **atypical**, and **0-1 is called non-anginal**.
- The more positives, the higher the likelihood that this chest pain is anginal.
- The **classic description** is a **crushing, retrosternal chest pain** that will radiate **down the arm** and **up the jaw**.
- **Associated symptoms** are also useful. The presence of **dyspnea, nausea/vomiting**, or **diaphoresis** with the onset of the chest pain increases the suspicion of myocardial ischemia.
- Consequences of the infarct may also be identified. **Congestive heart failure** (pulmonary edema, JVD, poor distal perfusion) and **arrhythmia** (especially heart blocks and ventricular tachycardia) can be seen, but are often absent.

Diagnosis

Rule out the **most severe disease (STEMI)** first with a **12-Lead ECG** looking for **ST-segment elevations** or a new **LBBB.** STEMI goes to **emergent cath.** If **negative rule out NSTEMI with biomarkers (Troponin-I).** NSTEMI goes to **urgent cath.**

- If both the **troponins and the ECG** ar **negative,** you're **left considering** if thi **pain is coronary** in nature at all. This ca be determined using the stress test. If th stress test is positive, go to **elective cath.**



Treadmill	ECG
Pharm	Echo
	Nuclear

If the person **can't walk** for any reason, use pharmacologic stress (either dobutamine or adenosine)

If the person has a **normal ECG** use ECG
If the person has an **abnormal ECG** use Echo
If the person has an **abnormal Echo** or CABG, use Nuclear

agnostic Modalities

The stress test

Regardless of the mechanism used, it's looking for the same thing: ***evidence of ischemia*** **under stress.** *The goal is to get the patient to* target heart rate **(85% of their maximum)** and have them sustain it. The test is **positive** if here is **chest pain during stress** or the **maging modality is positive.** For ECG test, ook for **ST segment changes (T wave version or ST segment elevations).**

For the **Echo,** look for **dyskinesia (also called akinesis)** that is present on stress but absent at rest (this is at-risk but not dead tissue).

- **Nuclear stress tests** demonstrate **perfusion with Thallium.** The **reversibility (normal perfusion at rest, compromised with stress)** identifies **salvageable tissue.** Whenever the **stress test** is **positive,** the **next step is catheterization.**

2. Catheterization

- This is **the best test** for the diagnosis of coronary artery disease. It assesses the **severity of stenosis** AND helps rule out **Prinzmetal's angina (clean coronary arteries producing ischemia as a product of vasospasm - treat with CCB).**

Acute Treatment

- Patients presenting with angina need **Aspirin**, first and foremost.
- **Nitrates** can be given to **alleviate pain,** but must be avoided in **right-sided infarcts (II, III, AvF).**
- **Beta-blockers** reduce myocardial work and prevent ventricular arrhythmias (the thing that kills patients in the first 24 hours).
- **ACE-inhibitors** have long term benefits.
- **Statins** are the mainstay of therapy for cholesterol. If it's certain this is Acute Coronary Syndrome, **therapeutic heparin** and **clopidogrel load** should be used as well.
- Oxygen and morphine are used.
- Interventional management choices are **Stent** or **CABG**. The decision is made based on the severity of occlusive disease. If its really bad (i.e. requires multiple stents) do a CABG. If the atherosclerosis is global, distal, or microvascular then **medical management only** may suffice.
- For thrombolysis, either the administration of **tPA** (within **12 hours** of onset) or **heparin** is done only when catheterization is not available AND they are in an acute disease (STEMI).

Chronic Therapy

1. Adjust risk factors

a.LDL High potency statin. Old LDL goal < 100. Now, start statin.

b.DM tight glucose control to near normal values (**80-120** or **HgbA1 C< 7%**) with oral medications or insulin.

c.HTN regular control of blood pressure to **<140 /<90** with **Beta-Blockers** (reduce arrhythmias) and **ACE-inhibitors.** Titrate heart rate to between **50-65 bpm and 75%** of the heart rate that produced symptoms on stress test.

2. Reduce Risk of Thrombosis

Aspirin (Cox-Inhibitor) is the standard therapy.

Clopidogrel (ADP-inhibitor) can be used if ASA allergy.

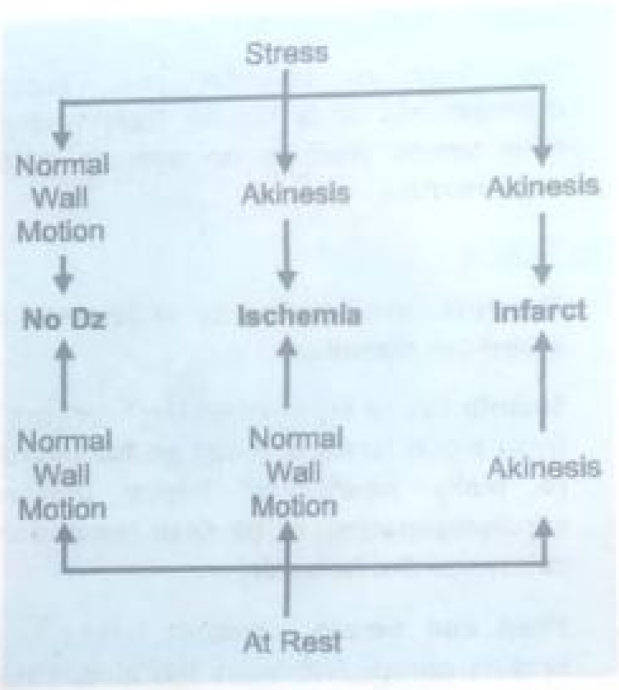
Can't Exercise:

Peripheral Vascular Disease, Claudication, vasculitis, diabetic ulcers, SOB at rest, etc.

Cann't Read ECG:

Any BBB or old infarct.

"Dead Things Don't Move"

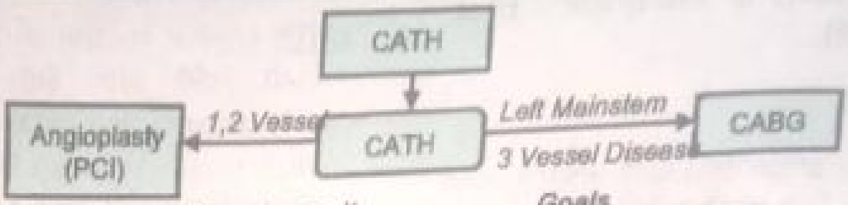


Acute Presentation: MONA-BASH

Morphine
Oxygen
Nitrates
Aspirin

Beta-Blocker
ACE-inhibitor
Statin
Heparin

Indication	*Duration*
Drug Eluding Stent	Clopidogrel x 12 months
Bare Metal Stent	Clopidogrel x 1 month
Angioplasty Alone	No Clopidogrel



Treatment	*When to use it*	*Goals*	
Statins	Any ACS	LDL < 70	HDL > 40
β-Blockers	Any ACS	SBP < 140	DBP < 90
ACE-i	Any ACS	SBP < 140	DBP < 90
ASA	Any ACS	No goal	
Clopidogrel	ASA allergy or stents	No goal	
Angioplasty	ST↑ or + Stress; 1 or 2 vessel disease		
CABG	ST↑ or + Stress; Left Mainstem 3 vessel disease		
tPA	ST↑; no PCI available, no transport		
Heparin	ST↑ or + Stress; contraindication to tPA		

Surgery = Left Mainstem OR 3-vessel disease; surgery = CABG
Angioplasty = 1,2 Vessel Disease

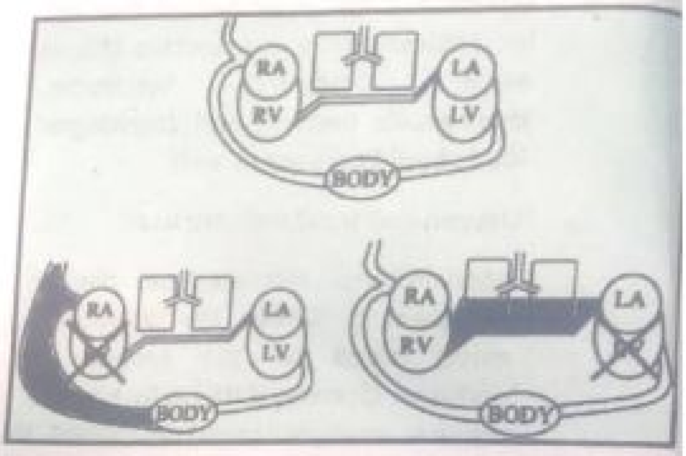
HEART FAILURE

Introduction

- Heart failure is enormously complex.
- There are multiple types, manifestations, causes, and treatments.
- You need to consider the chronic management of a regular heart failure then decide what to do with an acute exacerbation.

Types of Failure

- The first consideration to understand is **systolic** vs **diastolic**.
- **Systolic** failure arises when the heart can't push blood forward. It can go **backwards (a leaky heart)**, be **floppy (dilated cardiomyopathy), or be dead (secondary to myocardial ischemia)**.
- **Plain and simple - systolic failure** is a broken pump. The heart fills in diastole, hence, **diastolic failure** is when the heart **can't fill**. If something prevents the heart from relaxing and accepting blood it produces a diastolic failure. This might be from **hypertrophy or infiltration.**



Right failure = backup in the veins of the periphery

Left failure = backup in the veins of the lungs

The second consideration is left versus right failure.

- **Left Ventricular Failure** is a failure to pump blood into the periphery; there's a backup of blood into the lungs.
- **Right Ventricular Failure** causes a backup of blood into the venous circulation. Most of the time it's a combination of both.

Pathogenesis and Etiology

The typical chronic failure that occurs insidiously is **by** far the most common. It's caused by **hypertension**. High blood pressure causes an **increase** in systemic vascular resistance; the heart **has to pump** harder and harder to push the blood. **It gets** bigger and beefier to compensate. But just **like any** muscle, it putters out and eventually fails. **The heart gets** bigger, rounder, and eventually goes **floppy**. **Pathologically,** constant overstimulation by **catecholamines** first helps the heart overcome the hypertension. It eventually leads to **neural hormonal remodeling**, **cardiac toxicity**, and then **fibrosis**. Other etiologies are simply a matter of memorization.

Diastolic CHF (CHF with preserved ejection fraction) is caused by the things that prevent relaxation. Generally, it's a hypertrophic or restrictive cardiomyopathy. Pericardial disease and deposition disease can do it too.

Symptomatology

- Symptoms arise from where the fluid backs up.
- The **classic patient** is the triad of **Exertional Dyspnea, Orthopnea, and Paroxysmal Nocturnal Dyspnea**.
- **Exertional dyspnea** is shortness of breath limiting walking.
- **Orthopnea** is shortness of breath that's worse when lying flat.
- **Paroxysmal Nocturnal Dyspnea** is when the patient wakes up in the middle of the night gasping for breath. Because most patients have left and right failure together, **rales** (fluid on the lungs) may get mixed with **peripheral edema** and **hepatomegaly**.
- Symptoms like an **S3 heart sound** and **Jugular Venous Distension** are signs of **acute exacerbation**.
- **In the chronic setting,** it's critical to determine what **class** they are. Here, **we use NYHA**, as it directs treatment.

Failure	*Path*	*Etiology*	*EF*
Systolic Failure	**Forward** failure	**Leaky**valves = anyregurgitation **Dead** Heart=I schemia / infarction **Floppy**muscles = EtOH, HTN, Drug	⇩
Diastolic Failure	**Filling** failure	**Pericardium**= Pericardial Tamponade Constrictive Pericarditis **Cardiomyopathy** = Restrictive Hypertrophic	⇧

Symptoms

Left Ventricular Failure	Right Ventricular Failure
Orthopnea, Crackles, Rales	Hepatosplenomegaly, JVD
Dyspnea on Exertion, **S3**,	Peripharal Edema,
Paroxysmal Nocturnal Dyspnea	Dyspnea on Exertion, ↑JVP

S3 and JVD poor prognostic sign in acute exacerbation

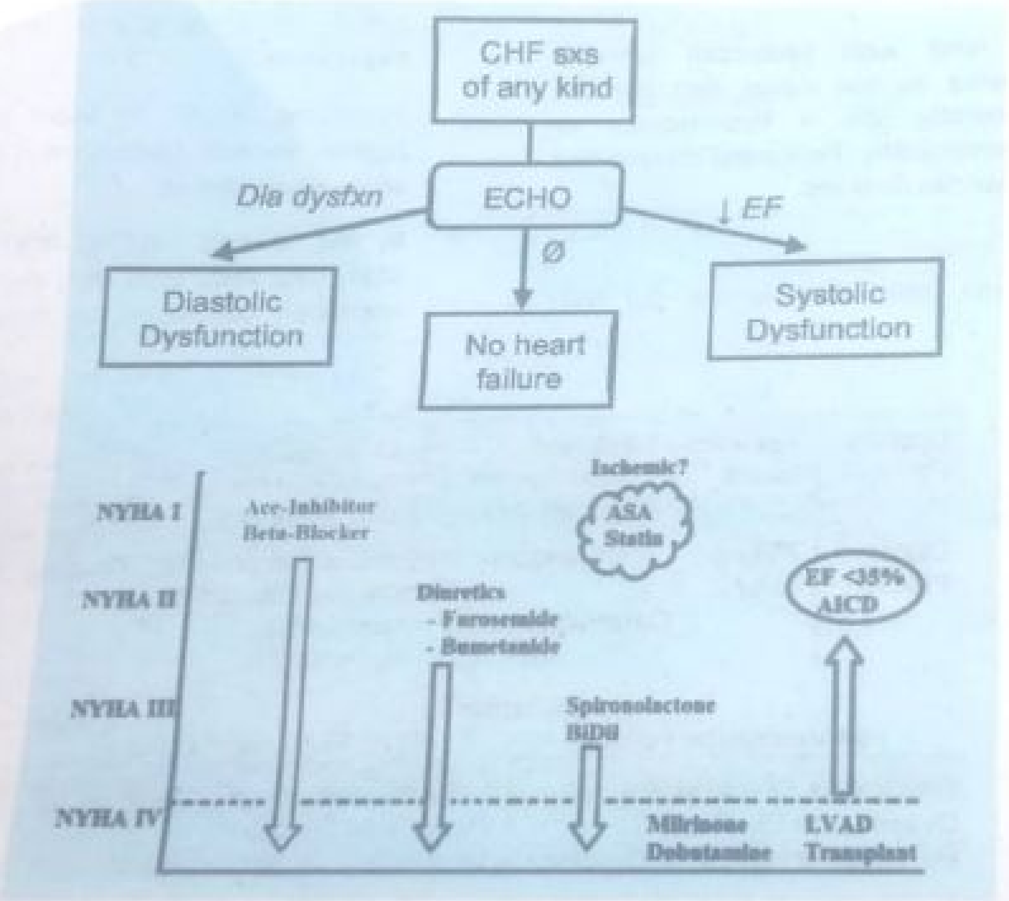
Chronic NYHA Class

I	Ø Limited	Ø Symptoms
II	Slight Limitations	Comfortable at **rest** and **walking**
III	Moderate Limitations	Comfortable at **rest only**
IV	Totally Limited	**Bed boundsxs @ rest**

The ACC/AHA has a class A D, based on the presence of structural heart disease. Don't use the A D model, use IIV

Diagnosis

- When first attempting to diagnose CHF there are two tests that should be used.
- The **BNP** is useful to say, **"volume overload or not."** It's a blood test and requires no advanced training to interpret.
- The **standard test** is the **2D echocardiogram**, which can ***distinguish between systolic failure (ejection fraction <55%) and diastolic failure (preserved ejection fraction).***
- There are more definitive tests available.
- A **nuclear study** calculates the exact ejection fraction and identifies areas of ischemia (it's a stress test).
- **Left Heart Catheterization** (even more definitive of EF and coronary artery disease) can be performed with a right heart cath to demonstrate elevated pulmonary artery pressures. ECG (demonstrates old ischemia / arrhythmia), CXR (demonstrates cardiomegaly or pulmonary edema), and troponins (acute ischemia) aren't inappropriate, but they're also not necessary.


CHF sxs of any kind
ECHO
Dia dysfxn
↓ EF
Ø
Diastolic Dysfunction
No heart failure
Systolic Dysfunction
NYHA I
NYHA II
NYHA III
NYHA IV
Ace-Inhibitor
Beta-Blocker
Diuretics
- Furosemide
- Bumetanide
Ischemic?
ASA
Statin
EF <35%
AICD
Spironolactone
ISDN
Milrinone
Dobutamine
LVAD
Transplant

Treatment with Reasoning

- *There are two goals: reduce fluid (preload) and reduce afterload.*
- ***To reduce fluid,*** *it's important to* ***restrict salt intake*** *(**< 2g/day** of **NaCl**) and reduce fluid intake (**< 2L H20/day**). Everybody gets this. Once the patient* ***reaches class II,*** keep the fluid off by using diuretics like **furosemide**. **At class III, Isosorbide Dinitrate** is added.
- Afterload reduction is achieved with **ACE-inhibitors** (also **Angiotensin Receptor Blockers**). When **CHF** gets really **bad (Class III and greater)**, add **Spironolactone** or **Hydralazine**.

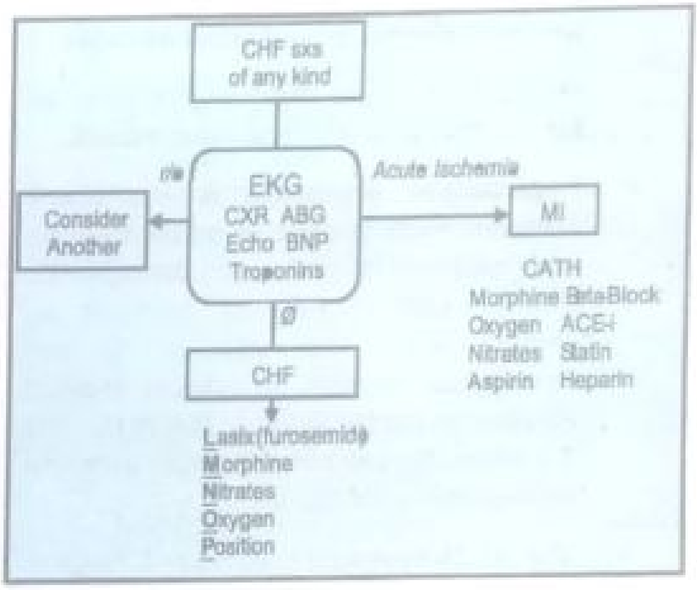
- **Isosorbide Dinitrate (preload)** and **Hydralazine (afterload)** are given as a combination medication BiDil®.

Patient	*Treatment*
Everybody	**Salt <2g** per day **H2O < 2L** per day **ACE-i** or **ARB** (best mortality benefit) **Beta-Blocker**
Preload Reduction	Diuretics such as **Furosemide** Nitrates such as **Isosorbide Dinitrate** Dietary Modifications (NaCl, H2O)
Afterload Reduction	ACE-i or ARB Hydralazine Spironolactone
Special	***Treatment***
EF < 35%	**AICD** (must be Class I-III)
Ischemic	**ASA** and **Statin**
Class IV	**Inotropes** like **Dobutamine** (ICU) VAD bridge to transplant **Transplant**

- When the situation is **dire (class IV)** it's time to add **inotropes** like **Dobutamine** (which is a continuous infusion) while preparing for a **transplant** or **ventricular assist device** bridging them to transplant.
- Ambulatory infusion devices are available.
- *To reduce the risk of sudden cardiac death,* **Beta-blockers** are used to reduce arrhythmia and neuro-hormonal remodeling.
- Other considerations are the placement of an **AICD** if the **EF < 35%** and they're **NOT class IV.**
- **Digoxin** can be used if there's need of symptom relief (knowing it won't change mortality).

Acute Exacerbation

- The precipitant of a CHF exacerbation (which usually means **volume overload**) can be a product of **dietary noncompliance**, **medication noncompliance**, blood pressure control, **ischemia** or **arrhythmia**.
- ***The goal is the same as for chronic management:*** **afterload reduction** (aka blood pressure control) and **preload reduction** (diuresis and nitrates).
- Ruling out acute ischemia (which should be treated as an MI) and other causes of dyspnea is **important**.
- But the person who is overtly overloaded (**JVD, crackles, peripheral edema**) with an **elevated BNP** needs aggressive diuresis with **IV Furosemide** and blood pressure control.
- ***Never start or increase a Beta-Blocker during an exacerbation.***



HYPERTENSION

Introduction

- **Hypertension**, high blood pressure, is defined by a **systolic blood pressure >140** or **diastolic blood pressure > 90** mmHg.
- Hypertension itself is a **silent disease; the patient doesn't feel it.** But it's a risk factor

for atherosclerotic diseases: peripheral vascular disease, stroke, heart attack.

- The goal is to modify this risk factor, to gain control of the disease, and to prevent development of heart disease.

Diagnosis

- Hypertension is diagnosed with **two separate blood pressures** taken at **two separate office visits** with the ***systolic or diastolic blood pressure being elevated.***
- The **best form of diagnosis** is *ambulatory blood pressure monitoring*, though since the *vitals are taken at each office visit*, it's often diagnosed in clinic.
- **According to JNC-8,** there is no more staging of hypertension, though that discussion is still included at the end of this topic with an explanation for why it is useful.
- **Hypertensive urgency** is any **blood pressure >180 systolic or >110 diastolic without evidence of end organ damage.**
- This is seen in the clinic, urgent **care, or ED.** It's managed with **oral medications.**
- **Hypertensive emergency** is any **blood pressure >180 systolic or >110 diastolic with evidence of end organ damage.** It's treated with *intravenous infusions to control MAP. The goal is to use intravenous nitrates or calcium channel blockers to get the MAP ↓ 25% in the first 2-6 hours, then to normal ranges with oral medications in 24 hours.*
- The 20, 10 symptom rule, Stage I, Stage II, urgency, and Emergency *because it suggests how many medications you'll need to gain control + JNC-7 focused on comorbid conditions. This is included to the right.*

JNC-8 Management

- *JNC-8 has made the management of hypertension quite simple.*
- While hypertension often exists with comorbid conditions that require stricter blood pressure goals, JNC-8 has clarified the management of hypertension.
- The **goal** for **Age ≥ 60 is 150/90, and for everyone else 140/90.**
- **To treat,** use your choice of **CCB** (Amlodipine), **Thiazide** (HCTZ) or **Ace-I.**
- If they **can't tolerate an Ace,** an **ARB** can also be used. It doesn't matter which is chosen or in which order.
- **Except: old people** (>75) and **African Americans** don't get an Ace-I / Arb to start.
- **Except: CKD** (even if you are old or AA) patients get an Ace-I / Arb as the first medication.

Stage	*SYS*	*DIA*	*Initial Tx*
Normal	120	80	Lifestyle and Diet
Pre-HTN			Lifestyle and Diet
Stage I	140	90	Thiazide > ACE > CCB
Stage II	160	100	Comorbid Specific
Urgency	180	110	PO Meds (Hydralazine)
Emergency	Alarm Sxs		IV Meds (Labetalol)

Start with Normal. Add 20 to systolic, 10 to diastolic to reach the minimum BP required for the next stage. It is an "OR" statement – if either the SYS or DIA is in a stage, you call it the highest qualified stage.

Dz	*Medications*
CAD	BB + Ace ... ISMN, CCB
CHF	BB + Ace ... ISDN + Hydralazine, Spironolactone
CVA	Ace-I
DM	Ace-I

CKD	Ace-i… Thiazides don't work after Cr > 1.5

Comorbid conditions often dictate the medications chosen, and may be directly opposing JNC-8 recommendations (CAD and CHF in particular)

JNC-8 Recommendations in a Nutshell

1. **≥60 + No Dz** = 150 / 90
2. Everyone else = 140 / 90
3. CCB, Thiazide, Ace/Arb
4. Old (>75) or AA = No Ace-i
5. CKD → Ace/Arb (overrides #4)
6. Don't use Beta-Blockers for Hypertension

Medications

You should learn the indications, contraindications, and side effects of each of the medications.

Major highlights that are worth remembering:

Class	*Side effect*	*Indication*
CCB	Peripheral	Edema JNC-8, Angina
ACE	↑ K, Cough, Angioedema	JNC 8 AA X Old X CKD Y
ARB	↑K	JNC-8 Ace-intolerance
Thiazide	↓K JNC-8 Stop if GFR ↓	
Loop	↓K	Renal Failure CHF II-IV
Beta Blocker	↓HR	CAD, CHF
Art Dilators	Reflex Tachy	CHF
Venodilator	Sildenafil unsafe drop in BP	CHF
Aldo Antagonists	↑K, Gynecomastia	CHF
Clonidine	Rebound HTN	NEVER USE

Ace-I induce ***angioedema***. If they do, the person must never again be on an ACE. **ARB is ok.**

Ace-I induce a **chronic dry cough**. Switch to an ARB if this happens. Both ACE and ARBs cause **hyperkalemia**.

Beta-blockers reduce the heart rate. While it's considered a side effect, it's often intended (as in CHF and CAD) to reduce the workload of the heart.

Spironolactone causes gynecomastia and hyperkalemia. If the gynecomastia becomes a problem, switch to eplerenone.

Secondary Hypertension

Rather than attempt to impart all the nuances of the differential for secondary hypertension here, which would certainly be overwhelming, we introduce the topic and expect you to be able to identify someone who may have secondary hypertension.

Hypertension **before the age of 35** (though this has been challenged by the **rise of childhood and early adult obesity**) or any hypertension that's **refractory to 3 medications** where one is a diuretic should be considered for secondary causes. As the **fourth medication** is reached, alternative causes should be considered.

The most common secondary cause is **CKD / ESRD**. If the patient has this condition no workup need be done.

If they don't, then the tests to do and the order to do them in is dependent on the clinic picture. Assessing for clues in the history, physical, and typical labs guide where to start.

Class	*Examples*
CCB	Amlodipine, Felodipine
ACE	Lisinopril, Quinapril, Benazepril
ARB	Losartan, Valsartan
Thiazide	HCTZ, Chlorthalidone
Loop	Furosemide
Beta Blocker	Metoprolol, Carvedilol, Nebivolol
Art Dilators	Hydralazine
Venodilator	Isosorbide Dinitrate, Mononitrate
Aldo	Spironolactone (gynecomastia)
Antagonists	Eplerenone (no gynecomastia)

Conn's (Primary **Hyperaldosteronism**), **Pheochromocytoma**, and **Cushing's**. **Renovascular Hypertension** and **Aortic Coarctation** are also discussed in following table.

Type	*History*	*Workup*
Hyperaldo (1o Aldo)	Refractory HTN or HTN and HypoK	Aldo:Renin > 20 CT Pelvis
Hyperthyroid	Weight Loss, Sweating, Heat intolerance, Palpitation,	TSH, Free T4
Hypercalcemia	Polyuria, AMS, "moans, groans, bones, kidney stones"	Free Ca
Aortic Coarctation	Children = warm arms, cold legs, claudication Adults = Rib notching, BP differential in legs and arms	X-ray of Chest Angiogram, CT Angio
Renovascular	DM or glomerulonephritis Young woman = FMD Old guy = RAS Renal Bruit, Hypo K	CrCl BMP Aldo:Renin < 10 U/S Renal Artery
Pheochromocytoma	Pallor, Palpitations, Pain, Perspiration, Pressure	24-Hr Urinary metanephrines, CT
Cushing's	Diabetes, HTN, Central obesity, Moon Facies	Low-dose Dexa ACTH Level High-dose Dexa
OSA	Obesity, daytime somnolence, improved with CPAP	Sleep Study

PERICARDIAL DISEASE

Introduction

- The etiologies of all pericardial diseases are the same.
- **Infections**, **autoimmune diseases**, **trauma**, and **proximate cancers** (lung, breast, esophagus, and mediastinum) cause pericardial disease.
- If **acute**, they cause an **inflammatory condition** (pericarditis). If they happen to **make fluid** they cause an **effusion**, or in its worst form, **tamponade**.
- If **chronic**, the inflammatory condition can be around long enough to cause **fibrosis**, which leads to **constrictive pericarditis**.
- Focus on identification and treatment rather than etiology.

1) Pericarditis

- Pericarditis is an inflammatory disease with an inflammatory treatment.
- It presents as **pleuritic** and **positional** ***(better when leaning forward)*** chest pain that will have a **multiphasic friction rub**.
- Caused by an inflammation of the sac around the heart, every heart beat causes irritation, producing constant pain.
- An **ECG** will show **diffuse ST segment elevation** ***(caution MI)***, but what is pathognomonic is **PR segment Depression**.
- **An Echo** will show an **effusion** but **not the inflammation.** Echo is the wrong answer.
- Theoretically, **MRI is the best radiographic test,** but is often not needed.
- The treatment is **NSAIDs + Colchicine**. There may be times where **either NSAIDs or Colchicine can't be used**; in that case **monotherapy is used.**
- **Steroids** are used in refractory cases, but associated with recurrence; they're usually the **wrong answer.**

Scanned with CamScanner

2) Pericardial Effusion / Tamponade

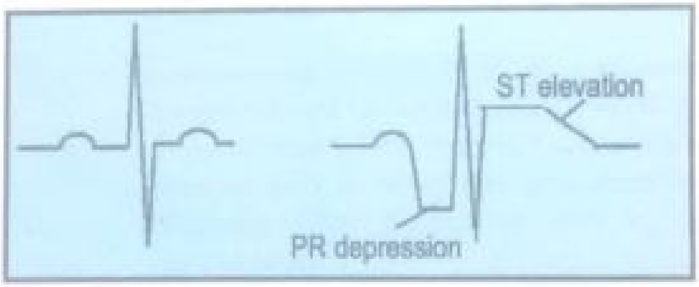
- When fluid accumulates in the pericardial space there's **pericardial effusion**.
- If that effusion is slowly developing **or small in size,** it may just be an incidental finding on echo. If it progresses quickly or gets large, there may be symptoms.
- These symptoms will be those of **CHF:** dyspnea on exertion, orthopnea, and PND.
- Diagnose the effusion with an **echocardiogram**.
- Pericardial effusions are secondary to an underlying cause.
- **Treat the effusion by treating the cause**. Most often an effusion develops in the setting of pericarditis; treating the pericarditis treats it. But if the effusion is **large, refractory, or recurrent** a **pericardial window (literally a hole in the pericardium)** can be made so that the fluid drains into the chest rather than into the pericardial space.
- If the effusion is **rapid** (or there's **ventricular hemorrhage)** the pericardium fills without time to compensate.
- This produces **tamponade.** Beck's triad **(JVD, Hypotension, Distant Heart Sounds**), clear lungs, and **pulsus paradoxus >10mmHg** make the clinical diagnosis.
- **Do EMERGENT pericardiocentesis.**
- An echo facilitates the diagnosis but is neither necessary nor sufficient.

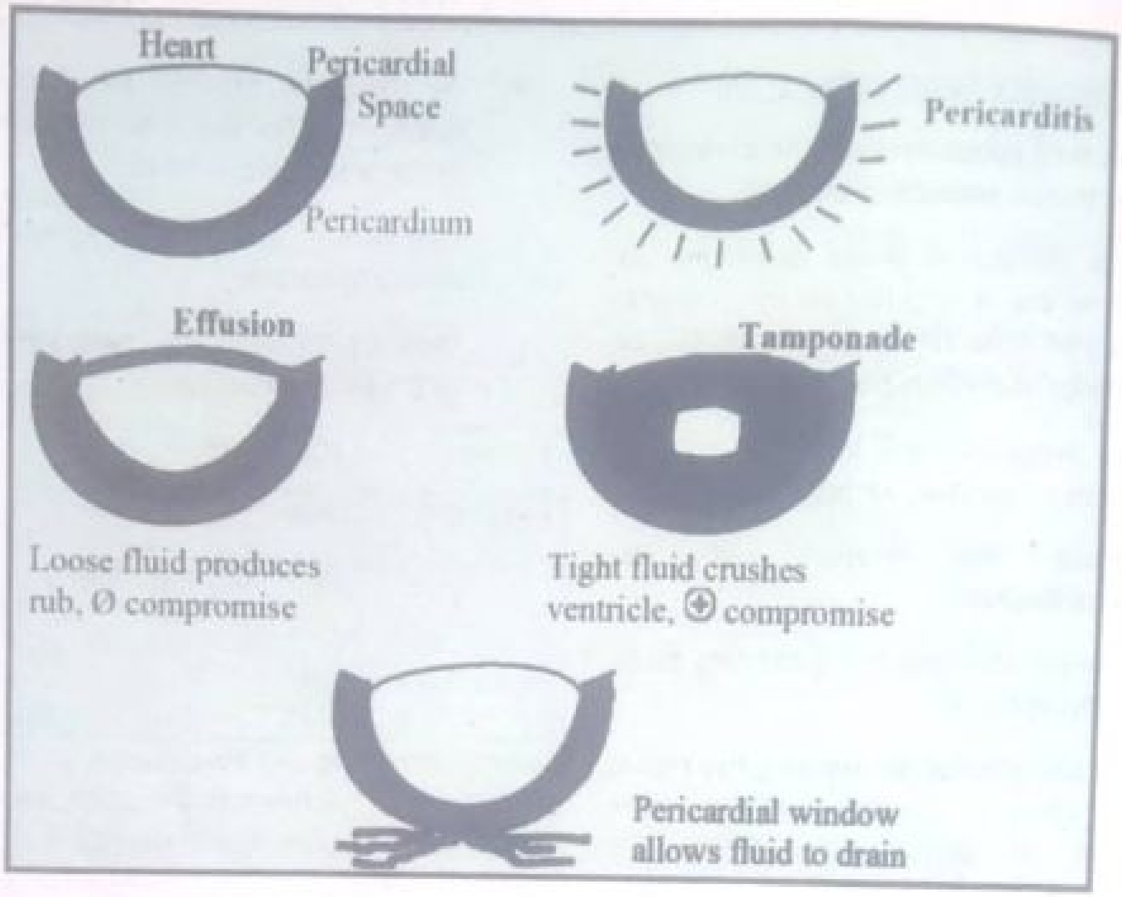
3) Constrictive Pericarditis

- If an inflammatory process is **left untreated long enough, fibrosis** will set in.
- The loose membrane of the pericardium becomes **fixed and rigid**.
- It causes no trouble with contractility, but the heart relaxes into a **rigid box**, limiting filling.
- As the heart expands into **too-small-a-space,** it strikes the walls of the box and causes a pericardial **knock**.
- Diagnosis is made with an **echocardiogram**.
- Treat by removing the rigid pericardium with a **pericardiectomy**.

Etiology	*Categories*
Infections	Viral (coxsackie) Bacterial (Strep/Staph) TB Fungus
Autoimmune	Lupus, Rheumatoid, Scleroderma Procainamide, Hydralazine, Uremia
Trauma	Blunt, Penetrating
Cancers	Lung, Breast, Esophagus, Lymphoma
Others	Many...

Disease	*Treatment*
Pericarditis	NSAIDs + Colchicine
Pericardial	effusion Pericarditis
Recurrent	Effusion Pericardial Window
Tamponade	Pericardiocentesis
Constrictive	Pericarditis Pericardiectomy

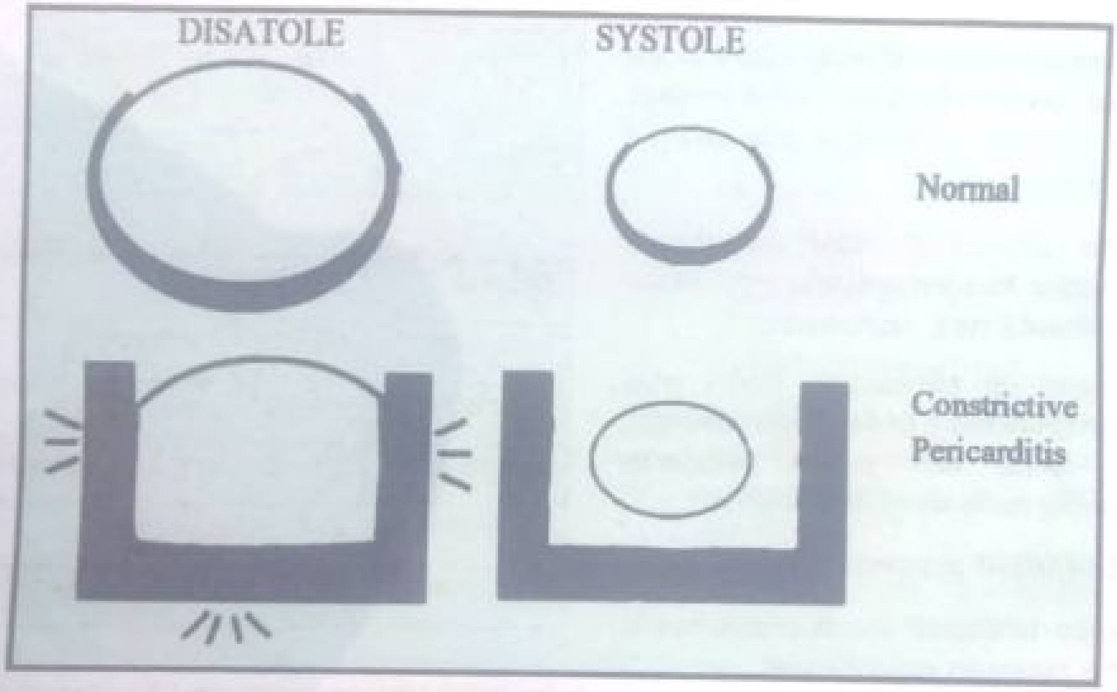



Heart
Pericardial Space
Pericardium
Pericarditis
Effusion
Tamponade

Loose fluid produces rub, Ø compromise

Tight fluid crushes ventricle, ⊕ compromise

Pericardial window allows fluid to drain


DISATOLE
SYSTOLE
Normal
Constrictive Pericarditis

SYNCOPE

Introduction

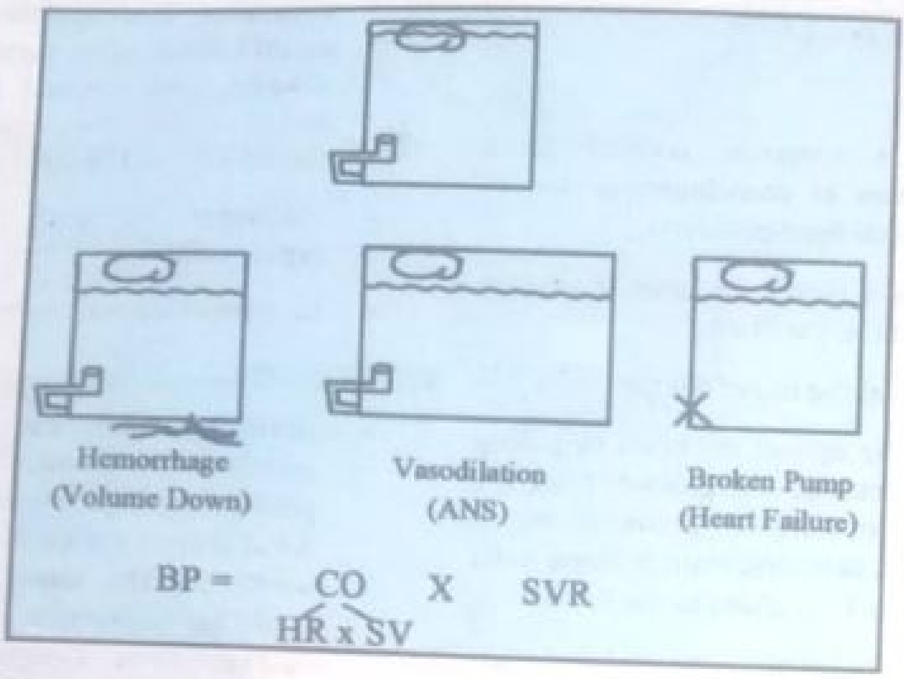
- Syncope's a symptom defined as a **transient loss of consciousness** due to global cerebral hypo perfusion.
- The heart is a pump; it pushes blood into the vasculature, the **"tank."**
- The brain is at the top of the tank.
- Gravity works against the heart by pulling the blood towards the ground. Thus, it's necessary to have a strong pump, a normal sized tank, and enough blood to fill the tank to get the blood to the brain.
- If blood **can't get up** to the brain, we pass out, i.e. **syncope.** It all comes down to **blood pressure** - a product of multiple factors **(equation to right).** The etiologies of syncope are vast; each affects one of these elements directly. But they all can be narrowed down to: a broken pump, too big a tank, and not enough fluid.
- It's important to realize how the history and physical relates to the potential etiology and the tests that need to be done to confirm suspicions.

eurocardiogenic (Vasovagal)

- The vagus nerve goes everywhere: **visceral organs, blood vessels, and the brain.**
- It's both **afferent and efferent**.
- Its signal to the blood vessels causes them to dilate, reducing systemic vascular resistance. The signal given to the heart is **bradycardia.**
- If the **Vagus nerve activates** more than it should (for whatever reason), it can cause **bradycardia** (cardio-inhibitory) or **hypotension** (vasodepressor). In both cases blood pressure falls, blood to the brain falls, and the person passes out.
- ***Lots of things can cause the Vagus to fire: visceral stimulation,*** such as **cough / defecation / micturition,** an **overactive carotid sinus** as in **turning the head** or **shaving,** and, because the vagus nerve comes from the brain, **psychotropic** causes such as the sight of blood.
- Vasovagal is both **situational** and **reproducible.**
- Do a **tilt-table** test to confirm suspicions.

Orthostatic Hypotension

- Normally, when going from sitting to standing the blood follows gravity and pools in the legs. The person does not feel it but there's a drop in blood pressure. It's sensed by the same baroreceptors that could go overactive in vasovagal. These carotids send a signal that causes an almost immediate compensatory vasoconstriction and increased heart rate (which is why we don't pass out every time we stand).
- But this reflex can fail if there's insufficient sympathetic tone or volume. If the **autonomic nervous system** is **broken** (as in the **elderly** or a **diabetic**) or there's something fighting against the sympathetic tone (such as **sepsis**) there can be **no reflex sympathetics** to compensate, causing a person to pass out. In other words – **SVR is insufficient.**
- However, if there's **insufficient preload** to begin with, standing up exacerbates the condition; CO is insufficient. A decreased preload is seen in people with **hypovolemia (diuretics, diarrhea, dehydration and hemorrhage).** In both cases **vital signs** are highly suggestive of the disease.
- A **decreased systolic BP of 20**, a **decrease diastolic BP of 10**, an **increase in HR of 10**, or symptoms when moving from a laying position to a standing one give away the diagnosis. This person is said to be **"orthostatic."**
- Give back the volume with **IVF** if volume's down, or give **pressors**.



- Overactive Vagus HoTN, Bradycardia
- Situational Syncope
  - Visceralà Cough, Defecation/Micturition
  - Turning Head/ Shaving
  - Site of bloodà Psychogenic
- Tilt Table

- Failure of Reflex Sympathetics
  - Elderly/DMà Broken ANS
  - Sepsisà Inflammatory Cytokines
  - Anaphylaxisà Same as sepsis
  - Addison's Disease
- Hypovolemia
  - Hemorrhage
  - Dehydration
  - Diuretics
- Postural Hypotension
  - Layingà Standing
  - SysBP↓ 20, DiaBP ↓ 10, HR ↑ 10
  - Rehydrate or Add Constrictors

Mechanical Cardiac Disease

- This is a *rare cause of syncope*.
- If there's a giant **obstruction to outflow** from the heart **(saddle embolus, aortic stenosis, HOCM, LA Myxoma)** the cardiac output suffers. Because the patient is living, syncope occurs with an increase in cardiac demand, i.e. **sudden onset with exertion**.
- There might be an **audible murmur,** but these diseases are structural so get an **Echo**.
- Cardiac output suffers because there's an obstruction to outflow. For a more thorough discussion of this phenomena please see hypertrophic cardiomyopathy in the cardiomyopathy section.

- StructuralLesion
  - PE, AS, HOCM, LA Myxoma
- Post Exertional Syncope
- ECHO
- Treatment Etiology dependent

- Sudden onset syncope, without prodrome
- Rapid change in CO
  - Too fast = ↓ Preload
  - Too slow = ↓ HR
- ECG à ECHO
- Antiarrhythmia or Defibrillator

Arrhythmia

- Arrhythmias are typically a disorder of **automaticity**.
- If the heart goes **too fast**, there's not enough time to fill (↓ **preload**).
- If the heart goes **too slow**, heart rate suffers + with it BP.
- Syncope will occur **suddenly**, without warning.
- An **ECG** will show the arrhythmia IF symptoms are occurring at the time of ECG, but it usually requires a **24-hr Halter** monitor to catch symptoms occurring with the arrhythmia.
- This will require **antiarrhythmics** or an **AICD** to flip them into a normal rhythm.

Neuro

- Some things **LOOK like a syncopal episode** but actually aren't.
- If you see someone **"pass out,"** consider these diseases.
- This section is even more brief than usual; ***only one neuro cause is actually syncope.***
- Decreased blood flow to the posterior circulation – **vertebrobasilar insufficiency** – may result in the patient passing out.
- Diagnose it with a **CT Angiogram** by looking at the vertebrobasilar arteries.
- If the patient is **post-ictal** after **"passing out"** they may have had a **seizure**.
- Diagnose with an **EEG**. If the patient has a **focal neurologic deficit** they may have had a **stroke**. Diagnose with a **CT** or an **MRI**.
- If the patient simply **falls asleep** and **wakes refreshed** consider **narcolepsy**; treat with **amphetamines** and regularly scheduled naps.
- *Put it in practice – handling syncope:* "Woman 3-2-1 PE"

	History	*Physical*	*Diagnosis*
VV (Vaso Vagal) - Visceral Organs (micturition, defecation, cough) - Carotid Stimulation (turning head, shaving) - Psychogenic (site of blood)	Situational, often Reproducible, with a positive prodrome	Vagal stimulation produces asystole or a ↓ SYS BP of 50 mmHg	Tilt Table
Orthostatics - Volume Down - Autonomic Nervous Dysfunction	Orthostatic Hypotension	Defined as ↓**SYS BP** by 20 ↓**DIA BP** by 10 ↑**HR** by 20 Sxs of orthostasis	Volume and Reassess, chase causes of hypotension if refractory to fluid
Mechanical Cardiac	Exertional syncope	Murmur	Echo
Arrhythmia	Sudden Onset, unprovoked,	None	24-hour Holter
Neuro (vertebrobasilar insufficiency)	Sudden Onset, unprovoked, very rare	Focal Neurologic Deficit	CTA
Pulmonary Embolism	PE	PE	Wells Criteria, CT scan
Electrolytes (bG, Tsh)	None	None	BMO

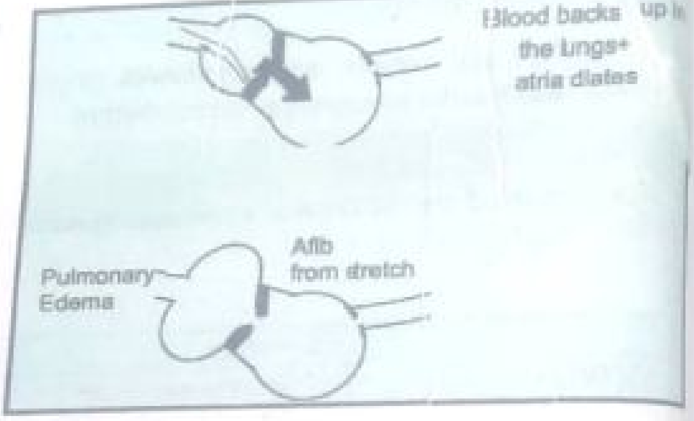
VALVULARDISEASE

Introduction

- Cardiac murmurs occur as a result from **increased turbulence**.
- They're caused by **increased flow across a narrowed lumen** - either from a **stenotic valve** or a **regurgitant** one. The **location** and **timing within the cardiac cycle** are useful for identification of the murmur before imaging.
- *Confirmatory diagnosis is always with* **echocardiogram**.
- The good *news* ***is not all murmurs are pathologic.***
- *If the* **murmur** is **< grade 3** (out of 6), **systolic**, and **asymptomatic** it needs no investigation.
- Any **diastolic, symptomatic**, or **> grade 3** requires a workup.
- The goal should be to identify on ***auscultation, understand treatment and maneuvers (which mirror one another), and then learn the nuances found on history or physical.***

Mitral Stenosis

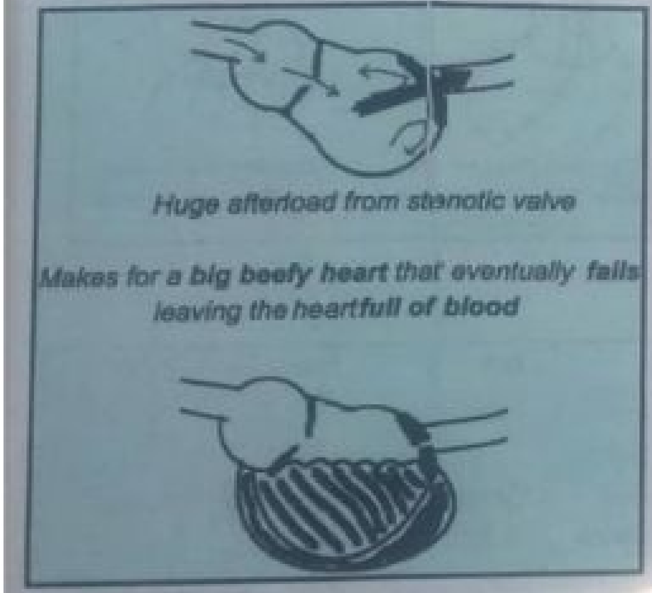
- *Mitral stenosis represents an* **obstruction to flow** across the **mitral valve** during **diastole**.
- *Atrial pressures are* **near to 0**, with blood normally just falling into the ventricle.
- Now forward flow is impeded - **blood backs up in the lungs** and you get **CHF / SOB symptoms**. Because there's also an **atrial stretch**, a resultant **Afib** is possible.
- *Caused almost exclusively by* ***rheumatic fever***, it's imperative that **strep throat** be treated appropriately.
- *The auscultation will reveal an* **opening snap** followed by a **decrescendo murmur** in **diastole** - the **worse** the stenosis th **earlier the snap.**
- Treatment is initiated when symptom begin.
- Do not wait for congestive heart failure t set in. ***Because more flow = mor murmur.*** treat this with **preloa reduction**.
- For *severe disease* **balloon valvotomy** o **valve replacement** is required. If there i **resultant afib, anticoagulate** an **cardiovert** after the lesion is identifie Commissurotomies aren't performe anymore.



Aortic Stenosis

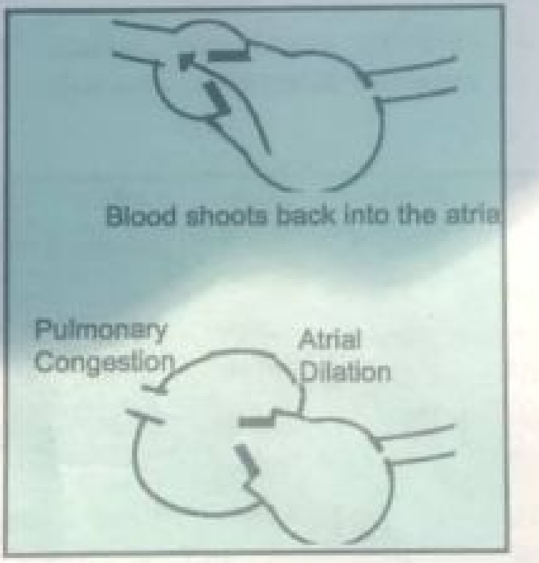
- Aortic stenosis is an obstruction in getting **blood out** of the ventricle during **systole**. Because the most common cause is **calcification** (even in the case of congenital bicuspid valves, where calcification is just accelerated), and calcification takes decades to set in, this disease occurs in **elderly men.**
- The **most common presentation** is **angina, especially on exertion** (*old men have coronary artery disease AND now they have calcification too).*
- **Syncope** is classic, especially as cardiac demand increases (as in with exertion). The **worst symptom** is active **CHF**, implying the worst prognosis - **a 1-3 year survival from diagnosis.**

- Heard best at the **aortic region,** it's a **crescendo-decrescendo** murmur. Because it will cause hypertrophy and eventual failure (as the left ventricle pushes against an enlarged "afterload"), treatment is a must.
- Start with **preload reduction** so there's less to push.
- A **valve replacement** is required sooner rather than later. In this case, a commissurotomy or valvotomy is not possible, because the calcifications are too thick. A valve replacement will result in the **ostia** being lost; it prompts a **CABG** regardless of CAD status.


Huge afterload from stenotic valve
Makes for a big beefy heart that eventually fails leaving the heartfull of blood

Mitral Regurgitation

- Blood should **exit the left ventricle** though the aortic valve.
- The mitral valve prevents it from going back into the atria. When the mitral valve **fails,** blood shoots from the high pressure left ventricle to the low pressure left atrium. This causes **atrial stretch** (potential Afib), **pulmonary congestion** (full blown pulmonary edema to CHF), and a **decreased forward flow** (cardiogenic shock). The process may be **acute** (rapid, sudden, devastating) and is a result of valve destruction. *Causes include* **ruptured papillary muscle** or **Chordae Tendinae** (via myocardial ischemia), **infective endocarditis**, or direct trauma.
- Onset will be **sudden** and the symptoms **fulminant**. Rapid identification and surgery is required.
- In the **chronic** (slowly developing - time for compensation) condition, usually secondary to **ischemia** or **mitral valve prolapse,** the onset is **gradual** and the symptoms are simply **exertional dyspnea** or **fatigue**.
- Heart failure may be controlled with normal medications, but **replace before CHF / Afib / Dilation** occur.
- Treat it when it's found.
- This is the classic **holosystolic murmur radiating to axilla** heard best at the **cardiac apex**.

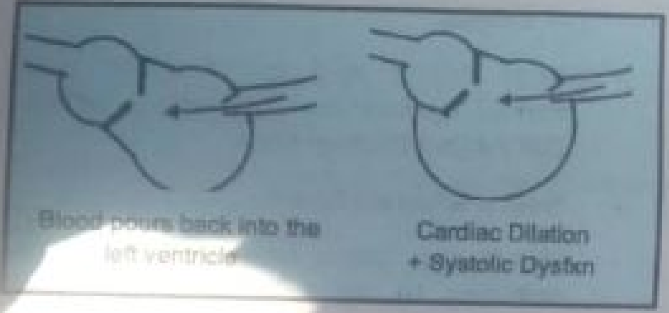


Aortic Insufficiency

- Blood **should not fall back** into the left ventricle **during diastole**.
- In fact, **aortic contraction** maintains **diastolic blood pressures.**
- If the aortic valve is floppy (**ischemia** or **infection**) as the aorta's contractility squeezes blood, it will squeeze it back into the ventricle rather than forward into the periphery. This presents with **dilated heart**

failure if chronic or **cardiogenic shock** if acute.

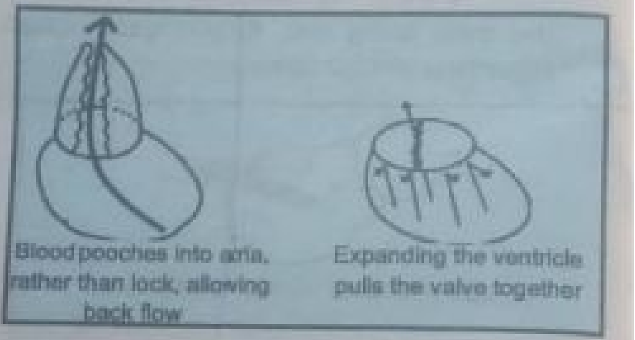
- **Some end-stage findings** have been characterized and named. Impress the attending with their knowledge but the valve should be **replaced** before that happens.
- This is a **decrescendo murmur** heard best at the **aortic valve**.

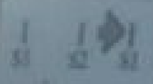
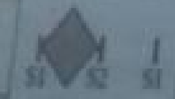
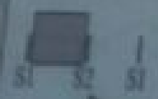
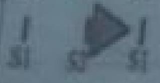
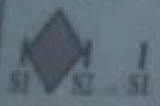
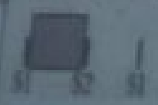

Blood pours back into the left ventricle
Cardiac Dilation + Systolic Dysfxn

[illegible]

Generally, mitral valve prolapse is a congenital defect of the valve leaflets.

- They are **too big** for the annulus; they pooch into the atria.
- The murmur sounds like **mitral regurgitation** but the pathogenesis and treatment is far different.
- Expanding intravascular volume and allowing the heart to fill will stretch the annulus and make the leaflets fit better.
- Look for the **pregnant woman** (whose decreased venous return exacerbates this murmur).


Blood pooches into atria, rather than lock, allowing back flow
Expanding the ventricle pulls the valve together

	Murmur	*Location*	*Leg Raise*	*Valsalva*	*Tx*	*Path*	*Presentation*	*Def Tx*
Mitral Stenosis		Apex	Worsens	Improves	Preload Reduction	Rheumatic Fever	Afib, CHF SOB	Replace
Aortic Stenosis		Aortic to Carotids	Worsens	Improves	Preload Reduction	Calcification Bicuspid	Angina, CHF Syncope	Replace
Mitral Regurg		Apex to Axilla	Worsens	Improves	Preload Reduction	Infxn Infarction	CHF	Replace
Aortic Regurg		Aortic	Worsens	Improves	Preload Reduction	Infxn Infarction	CHF	Replace
HCOM		Apex	Improves	Worsens	Increase Preload	Congenital	SOB, Sudden Death	Replace
Mitral Valve Prolapse		Apex	Improves	Worsens	Increase Preload	Congenital	CHF	Replace

DERMATOLOGY

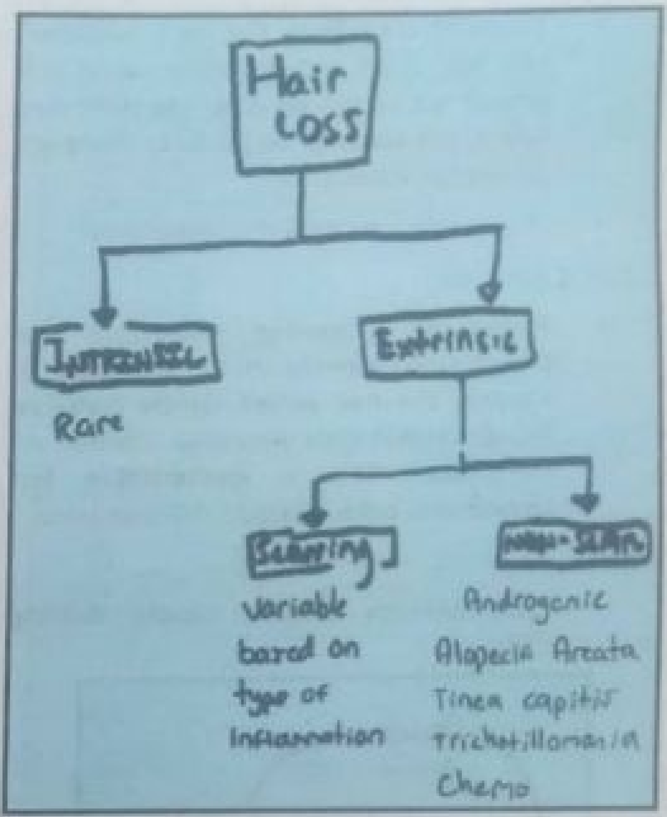
ALOPECIA

Male Pattern Baldness – Androgenic Alopecia

- Hair follicles are programmed to miniaturize under post-pubertal androgens.
- This is a common disease in men; it's largely considered cosmetic.
- The top of the head (the crown) begins to thin.
- Eventually, hair loss predominates. **5-DHT** is implicated in the pathology.
- Initial therapy is with **Minoxidil** topically and **finasteride** orally.
- Women with hyperandrogenism can suffer as well; they're treated with **OCPs** (suppress ovarian production of hormones) and **spironolactone.**

Alopecia Areata

- A systemic **autoimmune disorder against hair follicles**.
- It creates a **well-defined circular bald spot**.
- Also look for the exclamation **point** sign - small hairs within the bald-spot that appear to be floating because the hair shaft gets progressively narrower and loses pigment close to the scalp.
- The disease is treated with **steroids** – topical, intralesional, and systemic depending on severity.


Hair loss
Intrinsic
Rare
Extrinsic
Scarring
Variable based on type of Inflammation
Non-Scarring
Androgenic
Alopecia Areata
Tinea capitis
Trichotillomania
Chemo

Tinea Capitis

- A superficial **fungal infection** caused most commonly by Trichophyton tonsurans.
- It also causes a **circular bald spot with all hairs at equal length**.
- A **KOH prep** must be ordered to visualize the fungus; Trichophyton **doesn't** fluoresce under Wood's Lamp.
- Treat with **oral Griseofulvin** (note NOT topical) – failure to do so will result in permanent hair loss.

Trichotillomania

- A **psychiatric** disease whereby the patient compulsively pulls out hair one strand at a time.
- There is a high association with anxiety disorders (PTSD, OCD, MDD).

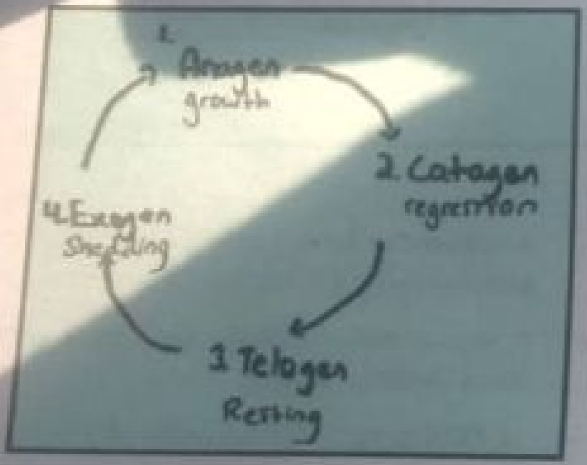
- The vignette will always give you a **woman**. Since she pulls hair out in different regions at different times, there'll be **patchy alopecia** with hair regrowth at **different lengths**.
- Diagnosis is made by shaving a **"window"** into her scalp and assessing equal hair growth within the window; the regrowing hair is too short to be plucked, hence it's allowed to grow.
- Treatment is to treat the compulsion.

Traction Alopecia

- Permanent **scarring** resulting in permanent **alopecia** that's secondary to keeping the hair **pulled tightly** (extreme braiding) that puts excessive traction on the root. This is **preventable** but **irreversible** once it occurs. RIP man buns.

Chemo

- Chemotherapy targets rapidly dividing cells.



- This means the cancer but also the gut (diarrhea), bone marrow (anemia, infection), and hair.
- Hair loss is expected, anticipated, and without treatment.
- **Anagen-effluvium** is when chemo disrupts growth, producing thin fragile hairs that shed with light touch, effectively skipping from anagen to exogen.
- **Telogen-effluvium** shifts anagen hairs to telogen; thinning the hair as the hair follicles exit growth phase too early.

Pemphigus Vulgaris

- Pemphigus is an **autoimmune disorder** against **desmoglein**.
- It's present in **desmosomes** that interconnect the epithelial cells of the epidermis.
- Because the destruction is between epithelial cells (**intra-epidermal**), the blister is **thin** and **tears easily** (**Nikolsky's Sign**).
- Diagnosis is made by **biopsy** showing a **tombstone** effect as basement membrane cells remain attached while epithelial cells split apart from each other.
- **Immunofluorescence** reveals **antibodies** on **epithelial cells throughout** the skin lesion. Because it's an autoimmune disease, treatment starts with **systemic steroids.**
- Once controlled, swap to **steroid sparing** immune modulators when possible (mycophenolate mofetil, rituximab).
- This disease is **life-threatening**, does **involve mucosa**, and occurs in people ages **30- 50**.

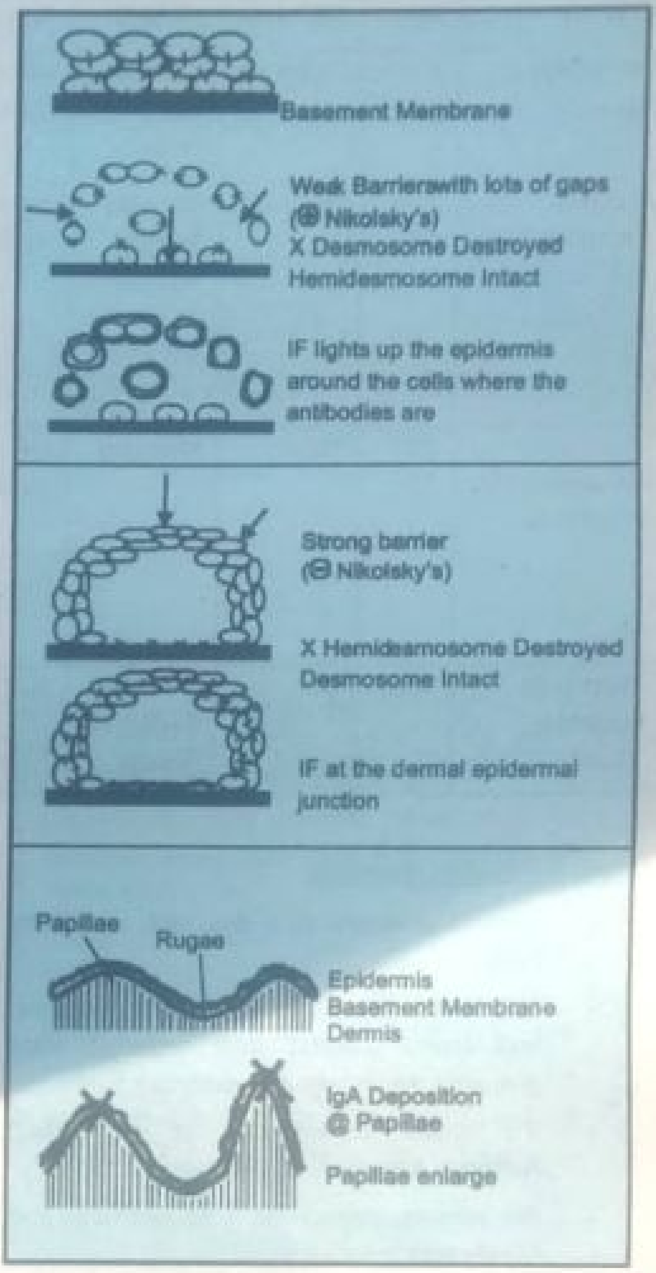
Bullous Pemphigoid

- Pemphigoid is another **autoimmune disorder**, this time against the **hemidesmosomes** that attach basement membrane cells to the basement membrane (**sub-epidermal lesion**).
- The detachment causes a **blister** but the intact epithelium results in a **tense, rigid bullae (Nikolsky's).**
- Again, a **biopsy** is used for diagnosis showing **intact epithelium** that's **detached from the basement membrane.**
- **Immunofluorescence** shows antibodies at the **dermal-epidermal junction**.
- Treatment is with **steroids** during acute attacks – topical for limited disease, systemic for severe.

- This **ISN'T** life threatening and **DOESN'T** involve the mucosa.
- It's most commonly found in ages **70-80**.

Dermatitis Herpetiformis

- This isn't a true blistering disease but is commonly tested against them.
- It's another **autoimmune disease** caused by **IgA antibodies** against **transglutaminase**.
- It's the **cutaneous manifestation** of **celiac sprue** and has the same pathology.
- The **antibody-antigen complex** gets deposited at the **dermal papillae** and causes an extension of the epidermis.
- It manifests as multiple small vesicular eruptions that are **pruritic** and found on the buttocks / legs or **extensor surfaces**.
- **A biopsy** is not needed, though if performed it'll show **"neutrophilic abscess."**
- Make the diagnosis instead by diagnosing the Sprue with anti-endomysial or anti-transglutaminase antibodies and an endoscopy.
- Treat the skin manifestation by treating the underlying disease: **remove gluten from diet** entirely.


Basement Membrane
Weak Barrierswith lots of gaps
(⊕ Nikolsky's)
X Desmosome Destroyed
Hemidesmosome Intact
IF lights up the epidermis around the cells where the antibodies are
Strong barrier
(⊖ Nikolsky's)
X Hemidesmosome Destroyed
Desmosome Intact
IF at the dermal epidermal junction
Papillae
Rugae
Epidermis
Basement Membrane
Dermis
IgA Deposition
@ Papillae
Papillae enlarge

Porphyria Cutanea Tarda

- The **most common porphyria disease**, it's the lowest yield of the **four.**
- **Bullae on sun-exposed** areas is highly suspicious for the disease.
- The diagnosis is made with **coral red urine under Wood's Lamp** caused by accumulation of urinary uroporphyrins.
- The underlying etiology is a **deficiency of uroporphyrinogen decarboxylase** but can be brought on by **OCPs, alcohol, Hep C, or Hemochromatosis.**
- **Avoid the sun.**

Disease	*Age*	*Mucosa*	*Blisters*	*Target*	*Dx*	*IF*	*Tx*
Pemphigus Vulgaris	40-50	Involved	Nikolsky Thin, Tears	Dermatomes (intracellular)	Bx	Within Epidermis	Steroids & MM
Bullous Pemphigus	70-80	No	Nikolsky Tense, Tough	Hemidesmosomes (to BM)	Bx	On Basement Membrane Epidermal-Dermal Junction	Steroids
Dermatitis Herpetiformis Porphyria	20-30	No	Nikolsky	IgA Deposition @ papillae	**Antibodies**	Deposition at the papillae (though this is not needed)	Remove Gluten from Diet
Porphyria Cutanea Tarda	**Any**	**No**	**Nikolsky Tense, Tough**	**N/A**	**Wood's Lamp**	**Don't do it**	**Avoid the sun**

Atopic Dermatitis (Eczema)

- Eczema presents as a **dry, red,** and **itchy** rash.
- **In infants,** it presents as papules, vesicles, and crusts (careful with impetigo) that presents on cheeks and extensor surfaces.
- It's almost always part of the **"3As," Asthma, Allergies, and Atopy**.
- **For infants,** deescalate food additions and slowly add food back.
- Avoid food that triggers a reaction.
- **In adults,** where the condition has been more chronic, there's **symmetrical lichenification** induced by a chronic itch-scratch cycle. Again, **avoidance of triggers (as with infants)** is crucial.
- **Topical emollients** can avoid the need for steroids.
- If **topical steroids** are prescribed, they may be used only for a brief time as they can lead to skin atrophy.
- The goal is to break the itch-scratch cycle and allow the skin to heal.

Contact Dermatitis

- There are **two forms of contact dermatitis:** ***irritant and allergic.***
- **Irritant** is caused by direct toxic effect of a chemical on the skin: i.e. excessive hand-washing, rubbing on leather boots, or some occupation-related chemical.
- Avoid those irritants and the patient should be fine.
- **Allergic** contact dermatitis is caused by a **Type IV hypersensitivity reaction** in response to some allergen.
- Common causes are metals like **Nickel *(on clothing or jewelry)*, latex,** or plants **(poison ivy / oak)**.
- Look for a red rash in the shape of an object (like a glove, bracelet, or shoe strap).
- Treat by avoiding contact with triggering agents and with topical **diphenhydramine** or aloe creams.

Stasis Dermatitis

- When fluid sits in a place for a long time chronic skin changes develop.
- So, for whatever reason, people with chronic lower extremity edema will develop stasis dermatitis.
- It's characterized by **edema, erythema, brown discoloration**, and **scaling** (flaking of skin).
- It's a **clinical diagnosis;** biopsy should be **avoided** as a non-healing ulcer may develop.
- Venous stasis ulcer (medial malleolus) can accompany stasis dermatitis.
- Early stasis dermatitis may mimic cellulitis, but is often the diagnosis when symmetrical and bilateral.
- Treatment is correcting volume overload (**diuretics only** when **overloaded**) and using **compression stockings** and **leg elevation** to facilitate drainage of fluid from the legs.

Hand Dermatitis

- Resulting from excessive hand-washing (look for the **food industry** or **health-care** worker).
- The dermatitis is on the **hands only.**
- The goal is to avoid frequent hand **washing** and **wear protective** gloves instead.
- Harsh hand soaps should be avoided. Moisturizers should be used frequently.

evi (Moles)

- Nevi are benign hyperplasia of **melanocytes.**
- Use the **ABCDE mnemonic** to ensure a benign lesion.
- (A)**symmetric**, **irregular Border**, **mixed Color**, a **large Diameter** (>5mm), or **Evolving** (changing over time) is suspicious of cancer and requires biopsy. **If anyone is positive, biopsy.**
- If **ALL are negative,** offer reassurance.
- There are **three kinds of nevi** depending on the layer the melanocytes are growing in.
- Be more concerned about whether it's ABCDE or not. What you care about is **melanoma**. Do a **wide excisional biopsy** and refer to the surgery skin cancer topic for more details.

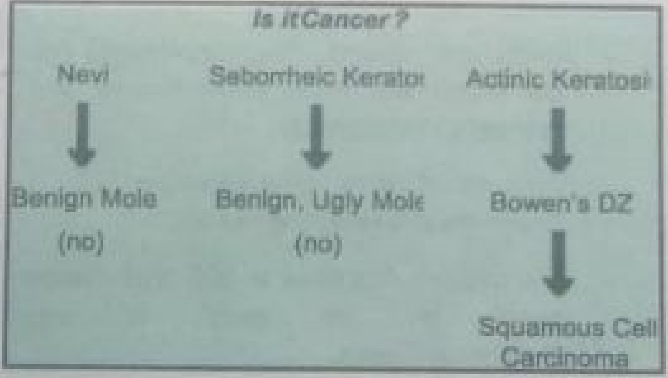
ABCDE = Cancer

- Asymmetric
- Irregular Border
- Mixed Colors
- Large Diameter > 5mm
- Evolving (changes in ABCD)

You need ANY 1 to suspect cancer

Seborrheic Keratosis (NOT Seborrheic Dermatitis)

- This is an **ugly looking mole** here to remind you that ***not*** all ABCDE is melanoma.
- These are often large, brown, **greasy looking**, and crusted.
- They look, "**stuck on**" the face of an **old person.**
- Here's the thing - it's a cosmetic mark of aging, but it can look an **awful lot like melanoma**. If it's been present for a ***long time and is unchanged,*** leave it be; it's *Seborrheic Keratosis.*
- If it's **new or changing,** do the **biopsy** to rule out melanoma. *Board exams can get tricky about this, so be careful.*



Actinic Keratosis

- A **premalignant** condition appearing as **erythematous with a sandpaper-like yellow to brown scale.**
- This is **squamous cell carcinoma** in the making and carries all the same risk factors.
- Look for the ***sun-exposed patient (farmer, sailor, burns early in childhood)*** and the ***sun-exposed area (face, arms, hands).***
- **Primary prevention** is key ***(wide-brimmed hats, sunscreen, avoidance of sun).***
- Local ablation with **cryosurgery** is ***first line treatment.***
- **5-FU** cream is used for diffuse lesions not amenable to cryosurgery.
- **Actinic Keratosis, Bowen Disease (carcinoma in situ), and Invasive Sqaumous Cell Carcinoma** are the same disease along a **common spectrum.**

Squamous Cell Carcinoma

- SCC is a locally invasive malignancy of keratinocytes that **can metastasize** (unlike basal cell).
- Risk factors are sun exposure.
- If it involves the lip, the lesion is almost **always on the lower lip**.
- The lesion itself will be fleshy, erythematous, and crusted or ulcerated.
- Biopsy the lesion, then perform **surgical excision.**

Keratoacanthomas

- Look and sound like squamous cell carcinoma but grow more rapidly and regress spontaneously.
- Because of their similarities to SCC, if found they're **resected** like SCC.
- If a patient describes a SCC that **"went away on its own"** it was **keratoacanthoma.**

Kaposi Sarcoma

- Malignancy of vascular endothelial cel that occurs with co-infection of **HHV-8** an **Immunosuppression (AIDS).**
- It's a **purple** lesion.
- Treat the AIDS and the tumors go away.
- Failure to resolve with HAART (rising CD4 implies the need for local or systemi chemotherapy. Also, they can b anywhere.

Urticaria

- Urticaria aka hives is a **Type Hypersensitivity Reaction**.
- Caused by exposure to an antigen, crosslinks **IgE** on **mast** cells causin **Histamine** to be released.
- This causes leaky capillaries, producing an **annular, blanching red papule** of varyin size.
- That antigen can be anything: ***bee sting, pressure, heat, food, contact dermatitis.***
- If there's **no anaphylaxis** a clinica diagnosis may be made; use anti-**histamines** to decrease the rash.
- Since any antigen can cause urticaria it' critical to identify the agent and avoi using it again.
- Send them to **RAST** to identify the culpri antigen.

Anaphylaxis = shortness of breath an hypotension with exposure to allergen. Giv epinephrine. Follow with systemic steroids, H1 blocker and H2 blocker.

Drug Reaction

- These are commonly a **pink, morbillifor** rash (though any rash may be the case occurring **7-14 days after exposure** (s new drugs are not culprits) in **hospitalize patients.**
- They're generally **widespread, symmetri** and **pruritic.**

- Always stop the offending agent.
- Give diphenhydramine for mild symptoms, corticosteroids for severe symptoms.
- A **fixed drug eruption** is any rash or blister that occurs in the same one spot in reaction to one drug every time it's administered.
- It occurs **within 24 hours** of **exposure**.
- Avoid the drug.
- It's never life-threatening.

Erythema-Multiforme

- This is primarily a **cutaneous** drug reaction to **medication** (Sulfa, Anticonvulsants, NSAIDs, and PCN) that appears as a **target shaped** lesion that can occur on the **palms and soles**.
- It's benign and **self-limited**.
- Remove the drug and watch.
- Two other possibilities to consider: **1** – It can be caused by **chronic HSV** and refractory cases need **acyclovir** and **2** – if it's spreading or involving the oral mucosa get ready for **Steven-Johnson Syndrome**.
- Syphilis may also present with Targetoid lesions on the palms and soles and might be present as a distractor on the tests.

Steven-Johnson Syndrome + Toxic Epidermal Necrolysis

- Both diseases are the same disease that exist as a continuum in severity commonly occurring from **drug reactions** (sulfa, anticonvulsants, NSAIDs, PCN).
- Each causes **widespread loss** of **sheets of skin** with a **+ Nikolsky Sign**.
- Two things differentiate the diseases: ***Body Surface Area + Biopsy.***
- **SJS** involves **<10% BSA** and has **basal cell degeneration** on biopsy.
- **TEN** involves **>30% BSA** and shows **full-thickness epidermal necrosis**.
- **Removal ALL meds** (including ***steroids***) and admit to the **burn unit** (heat, electrolytes, fluid, infection risk).
- The ***biopsy is critical to differentiate between*** the **SJS / TEN** (which responds to removal of antibiotics) and **Staphylococcus Scalded Skin Syndrome** (which responds to the administration of antibiotics), as well as separating ***severity of SJS versus TEN.***
- SSSS **doesn't have mucosal involvement.**

Dz	Pt	Tx	Bx
Urticaria	IgE-Mast Cell mediated release of histamine after exposure to any antigen, blanching red papule	Diphenhydramine, Epinephrine If Anaphylaxis	N/A
Drug Reaction	Widespread Symmetric pruritic rash OR Any One rash at One spot in reaction to One Drug	Stop the drug, monitor	N/A
Drythema Multiforme	Targetoid lesion on palms and soles caused either by HSV or will progress to Steven Johnson	Acyclovir and/or Remove Drug	N/A

Steven Johnson	<10% BSA affected + Nikolsky's, Oral Mucosal involvement	Admit to the burn unit, fluids, electrolytes, supportive care.	**Basal Cell Degeneration**
Toxic Epidermal Necrolysis	>30% BSA affected + Nikolsky, Oral Mucosal involvement	Steroids **AREN'T** helpful and may exacerbate the condition	Total epidermal thickness necrosis

HYPOPIGMENTATION

Introduction

- Finding a lesion on someone that's **Hypopigmented** isn't a big deal, but it's often the subject of board examinations.
- There isn't one algorithm to follow - just a loose group of associations to remember – which is perfect for building a summary table.

Tinea Versicolor

- **When there's a patchy depigmentation one of the things to consider is a fungal infection with Malassezia globosa.**
- **A normal fungus present in skin flora, it's unclear what causes it to overgrow, though Cushing's and Immunosuppression** are risk factors.
- Hypopigmentation is a result of inhibited melanin production.
- Patients present with **small scaly patches** of **varying color** (typically ***in summer***, as these spots don't tan).
- ***Diagnosis*** is made by **KOH prep** of the scale that reveals **hyphae + spores** that looks like ***"spaghetti and meatballs."***
- Treat with topical **selenium sulfide**.

Vitiligo

- An **autoimmune disease** that causes **small sharply demarcated depigmented macules** or **patches** with irregular borders that can coalesce.
- *They're usually found on the* **extremities, face**, and **genitalia**.
- Lesions can be picked up by the **Wood's Lamp Test** (no pigment at all), but *definitive diagnosis* is confirmed by the **absence of melanocytes** on histology.
- It's **associated** with **autoimmune disorders such as hypothyroidism** and **lupus.**
- Treatment is often ineffective.
- Steroids and UV light have been attempted.

Albinism

- If a patient is **completely white** with **pale hair** and **pale eyes** they likely have albinism.
- It's a **genetic disorder** of **tyrosinase** (normal melanocytes, deficient enzyme) so there is no treatment; the diagnosis is clinical.
- Simply protect these people from UV exposure and educate on preventing skin cancer.
- Albinism is tested against Piebaldism and PKU, which can result in pale-skinned kids.

- *Piebaldism is* ***Inadequate melanocyte migration*** *with a* ***white forelock*** *on the scalp)*
- *Albinism is* ***Inadequate tyrosinase activity****, total depigmentation in all surfaces*
- *PKU is a deficiency in phenylalanine hydroxylase, causing a* ***relative deficiency of tyrosine****. Screened for at birth. Intellectual disability, seizures follow if not for a special diet*

- *Shagreen patches (elevated fleshy collagen plaques)*
- *Adenoma Sebaceum (hyperplastic blood vessels).*

Ash Leaf

- A **child** with a single hypopigmented (**NOT depigmentation**) spot that's positive on **Wood's Lamp** is an Ash Leaf Spot and pathognomonic for **Tuberous sclerosis**.
- Watch for early onset seizures.
- Get a CT scan to visualize the tubers in the brain.
- Look for **Shagreen patches** and adenoma sebaceum.

Dz	Patient	Diagnosis	Biopsy	Treatment	Path	Risk Factors
Tinea Versicolor	Small Patchy Scales of varying color Back and Chest	KOH Prep "spaghetti and meatballs"	Ø	Topical selenium Sulfide	Overgrowth of fungus (normal flora)	Cushing's Immuno↓
Vitiligo	Macule or Papule on Hands and Face	Wood's Lamp enhances Lesion	Absent Melanocytes on histo prep	Ø tx Ppx vs Sun	Autoimmune	Other Autoimmune
Ash Leaf	Hypopigmented Lesion from birth	Wood's Lamp then CT	Ø	See Peds		

PAPULOSQUAMOUS RXNS

Seborrheic Dermatitis (NOT Seborrheic Keratosis)

- Think of this as super-dandruff.
- Dandruff is flaking of the scalp.
- It's treated with **selenium shampoo**.
- Seborrheic Dermatitis is a **fungal infection** that causes an inflammatory reaction in areas rich in sebaceous glands. That means **hair**.
- Look for a rash on the **scalp and eyebrows** that spares other areas of the face and ears.
- Treat with **selenium shampoo**.
- Topical steroids can be used as well if the inflammation doesn't settle with selenium
- Low-yield test associations include: **HIV infection**, **cradle cap** (infants), and Parkinson's disease.

Psoriasis

- Psoriasis is an autoimmune disease which causes proliferation of keratinocytes with excessive accumulation of the stratum corneum.
- It's thought to be caused by dysregulation of T-Helper cells.
- The patient will have **symmetric, well-demarcated silvery scales** that **bleed when picked** that commonly affect the scalp, gluteal fold, elbows, and knees.
- **Nail pitting** and onycholysis (detachment of the nail-bed) are common.
- If **joint pains** are present, consider Psoriatic Arthritis .

- The first step is **UV light** (sunlight or artificial exposure).
- **Topical steroids** are used in flares.
- Other agents, both topical and systemic (methotrexate, calcineurin-inhibitors, Anti-TNF-alpha).
- There MAY be the need to biopsy to rule out lymphoma **if the diagnosis is in question.**

Pityriasis Rosea

- A benign and self-limiting condition that resolves on its **own (~6 weeks).**
- We don't know what causes it.
- The disease begins with a **flat, oval, salmon-colored macule** (hyperpigmentation in darker skinned races) called the **herald patch.**
- The disease then progresses to **several salmon-colored scaling lesions** with a **trailing scale** (the scale does not reach the border of the salmon colored lesion).
- This will always **spare the palms and soles.**
- While it is self-limiting, it may be the presentation of syphilis; rule it out with an **RPR.** Involvement of the hands and soles *greatly* increases the chance of syphilis.

Lichen Planus

- Lichen Planus is an inflammatory disorder of unknown etiology.
- It causes an **intensely pruritic pink** or **purple** flat topped **papules** (you can feel them) with a **reticulated network of fine white lines.**
- It usually involves the wrists and ankles but may involve the trunk, the oral mucosa or the vaginal mucosa.
- Treatment is similar to psoriasis.
- **Topical steroids** are the mainstay of therapy, but should not be continued long term.
- **UV light** can be used as an adjunct (opposed to psoriasis where it's mo effective).
- Topical and systemic immune modulator are beyond the scope of this text.
- Be aware that a **lichenoid drug eruptio** (drug-induced lichen planus) can occu with Ace-I, thiazides, furosemide, an Beta-blockers.

Impetigo

- Commonly seen in children, this is caused by an infection with **Strep pyogenes.**
- Bullous impetigo is increasing in incidence and is caused by Staph aureus.
- Look for a **child** with **honey-crusted lesions** on the **face.** Impetigo can lead to **post-strep glomerulonephritis** but **NOT rheumatic fever.**
- Diagnosis is clinical, often in response to therapy if not just by the lesion itself.
- Treat **topically** (mupirocin) or with systemic antibiotics.
- **Any Beta-Lactam antibiotic (amoxicillin** or **1st gen cephalosporins)** is sufficient for the initial treatment of non-bullous impetigo.
- If bullous or there is no response, switch to **clindamycin.**

Erysipelas

- Commonly seen in adults, this is caused by an infection with **Strep pyogenes.**
- Erysipelas infects the lymphatics, so it'll be easy to see a **dark red, well-demarcated, indurated** lesion that outlines the lymphatics, appearing to **"climb up the extremity."**
- Treatment, like impetigo, starts with Beta-Lactams against strep (Amoxicillin) and escalates if there's no improvement.

Acne Vulgaris

- The most common dermatologic condition, it's caused by an infection by **Propionibacterium acnes.**

- It causes zits.
- Acne is a product of increased sebum production, follicular hyperkertinization, and colonization.
- It's a clinical diagnosis.
- The type of acne determines the approach to treatment.
- See this as "the worse the acne or the more refractory, the higher up the ladder you go." That ladder is topical retinoids, benzoyl peroxide, oral antibiotics, and isotretinoin. It is truly an escalation approach:

Not bad acne = retinoids

Teen cares about acne = benzoyl + retinoids

Acne won't go away = doxycycline

Scarring, nothing else has worked, severe = isotretinoin

Disease State	Treatment
Comedones (whiteheads, blackheads)	Topical retinoids
Inflamed Comedones or Pustules	Topical Retinoids + Benzoyl Peroxide
Severe Pustular or Nodulocystic disease	Oral Antibiotics (Doxycycline, erythromycin)
Severe Inflammatory or Resistant	Isotretinoin (UPT first)

- On the test, though, they'll give buzzwords that you should link with certain treatments. Rather than escalate, jump right to the treatment (see to the right).

Tinea infections

- **Tinea corporis** is infection on the body. Look for a round expanding plaque with moderate scaling and central clearing. It responds to topical antifungals
- **Tinea pedis** is infection of the foot. Look for interdigital maceration and scaling between toes. Treat with topical antifungals.
- **Tinea cruris** is "jock itch" and is a fungal infection of the groin. Treat with topicals.
- **Tinea ungulum** (onychomycosis) is treated with **oral** antifungals. Terbinafine is best, itraconazole is ok. Make sure you confirm the diagnosis with a KOH prep.

ENDOCRINOLOGY

ADRENAL GLANDS

Cushing's Syndrome

- A disease of **excess cortisol**, it's caused by one of four conditions:

  1) Iatrogenic (most common, taper off to fix),

  2) Pituitary tumor (Cushing's disease),

  3) Adrenal Tumor, or

  4) Ectopic ACTH.
- The patient will present with a **"Cushingoid appearance": central obesity, moon facies, extremity wasting**, a **buffalo hump, glucose intolerance** or **diabetes**, and **hypertension**.
- When faced with this condition, get a **24-hr free cortisol level** and confirm with **1mg Low Dose Dexamethasone Suppression test**.
- If cortisol is ↑+ it's Cushing's.
- Follow that with an **ACTH** level to distinguish adrenal (↓ ACTH) from extra-adrenal (↑ ACTH).
- If adrenal, spot it with a **CT/MRI** of the **Adrenals**.
- If extra-adrenal, perform a **high dose dexamethasone suppression test** to determine pituitary (suppresses) vs ectopic (Ø suppression).
- Confirm pituitary Cushings with an **MRI** followed by transsphenoidal resection.
- If ectopic, find it with **CT/MRI** of 1) Chest (**Lung Ca**),

  2) Abd (**Pancreatic ca**), then

  3) Pelvis (adrenals).
- Remember "Low-Dose ACTHen Hi Dose."

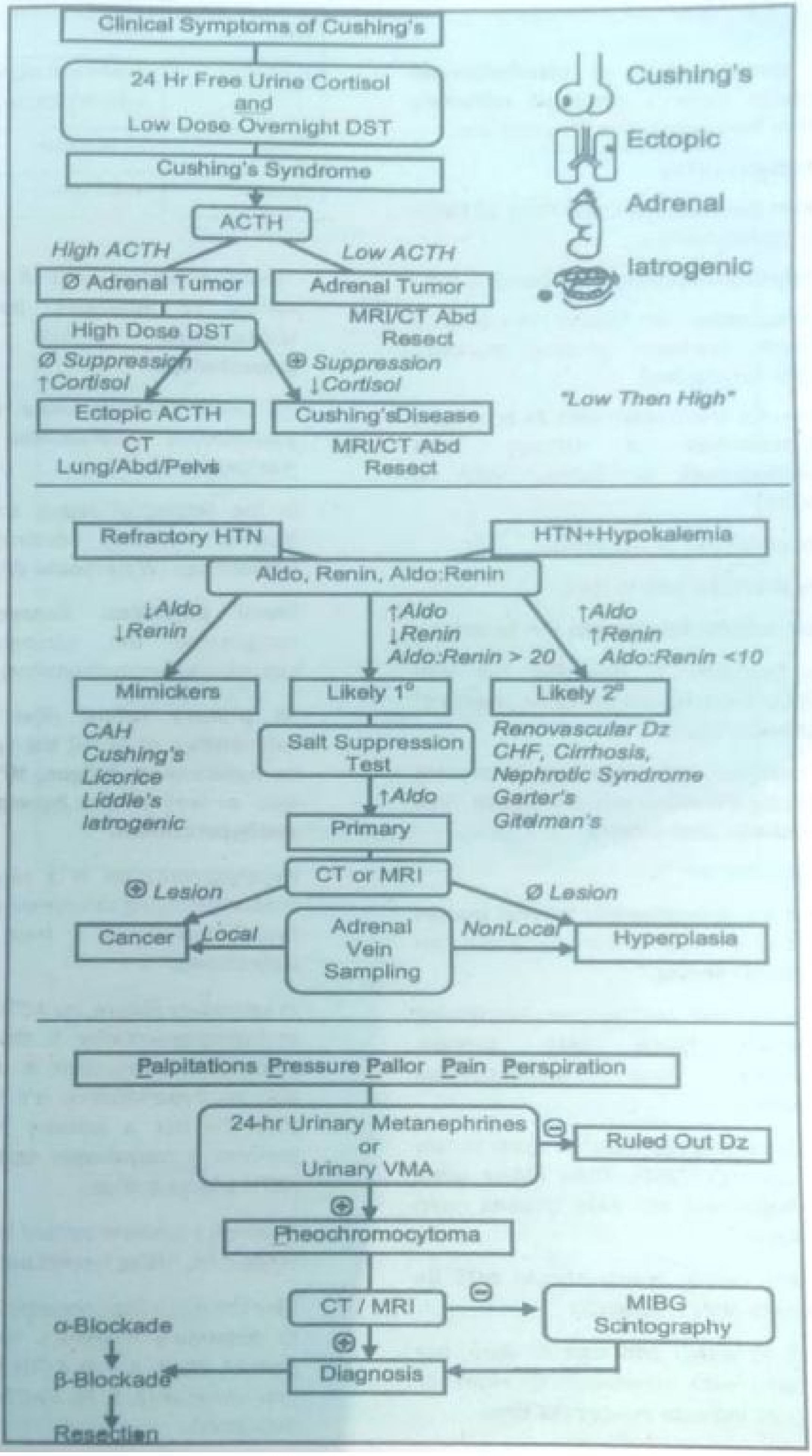
Hyperaldosteronism

- Aldosterone causes resorption of Na H_2O producing an expanded vasc volume and hypertension by ↑E_{Na} in collecting tubules, trading Na for K.
- This produces a **refractory HTN** or **Diastolic HTN and Hypokalemia.**
- ***Differentiate between:***

  Primary (a tumor or adenoma ca **Conn's Syndrome**) where aldosteron production is independent of Renin.

  Secondary (renovascular diseas edematous states of CHF, Cirrhos Nephrotic Syndrome) where th production of aldosterone is dependen on renin and is an appropriate response t ↓ renovascular flow

  Mimickers (CAG, Licorice, or exogenou mineral corticosteroids).
- When suspected, perform 8am levels fo **Aldosterone, Renin,** and **Aldo:Reni Ratio.**
- Ensure any hypertension medication i discontinued **(ACE, CCB, Diuretic confound the test).**
- If **elevated (>20 Aldo and >20 Aldo:Renin),** it's likely **primary.**
- Confirm with the **salt suppression** test (where aldo will not decrease after a 200g Na load).
- The tumor is found by **CT** or **MRI**.
- If early AM levels are **Ø elevated** a different disease is likely provoking the aldosterone increase.


Clinical Symptoms of Cushing's
24 Hr Free Urine Cortisol
and
Low Dose Overnight DST
Cushing's Syndrome
ACTH
High ACTH
Low ACTH
Ø Adrenal Tumor
Adrenal Tumor
MRI/CT Abd
Resect
High Dose DST
Ø Suppression
↑Cortisol
⊕ Suppression
↓Cortisol
Ectopic ACTH
CT
Lung/Abd/Pelvis
Cushing'sDisease
MRI/CT Abd
Resect
Cushing's
Ectopic
Adrenal
Iatrogenic
"Low Then High"
Refractory HTN
HTN+Hypokalemia
Aldo, Renin, Aldo:Renin
↓Aldo
↓Renin
↑Aldo
↓Renin
Aldo:Renin > 20
↑Aldo
↑Renin
Aldo:Renin <10
Mimickers
Likely 1°
Likely 2°
CAH
Cushing's
Licorice
Liddle's
Iatrogenic
Salt Suppression
Test
Renovascular Dz
CHF, Cirrhosis,
Nephrotic Syndrome
Barter's
Gitelman's
↑Aldo
Primary
CT or MRI
⊕ Lesion
Ø Lesion
Cancer
Local
Adrenal
Vein
Sampling
NonLocal
Hyperplasia
Palpitations Pressure Pallor Pain Perspiration
24-hr Urinary Metanephrines
or
Urinary VMA
⊖
Ruled Out Dz
⊕
Pheochromocytoma
CT / MRI
⊖
MIBG
Scintography
⊕
Diagnosis
α-Blockade
β-Blockade
Resection

Pheochromocytoma

- An overproduction of **catecholamines** produces either a **sustained refractory HTN** or **Paroxysmal Five P's** which are

  1) **Pressure** (HTN),

  2) **Pain** (Headache or Chest Pain), 3) **Pallor** (vasoconstriction),

  4) **Palpitations** (tachycardia, tremor), and

  5) **Perspiration.** This follows the rule of 10 percents (excellent pimping question, useless for practice).
- Screen for this disease with **24 hr urinary metanephrines** or **Urinary VMA** (**metanephrines** is better, VMA is cheaper).
- If do an **MRI/CT** of the pelvis.
- They should be easy to spot.
- If not, a **MIBG Scintigraphy** can be done.
- The treatment is **resection** but with caution; touching one can cause release of catecholamines.
- Pretreat first with **α-blockade** to prevent unopposed α-action with β-blockade, then **β-Blockade**, then **surgery**.

drenal Incidentalomas

- These are **asymptomatic adrenal masses** found on CT scan for something else - an **"incidental finding."**
- It's important to rule out **functioning** adenomas **(pheo, aldo, cortisol, androgen)** from **nonfunctioning** adenomas.
- **All above findings** must be done to rule out Cushing's (**DST**), Pheo (**24-hr urine metanephrines**) and Aldo (**plasma renin and Aldo**).

A direct needle biopsy should **NOT be** done until pheo is ruled out.

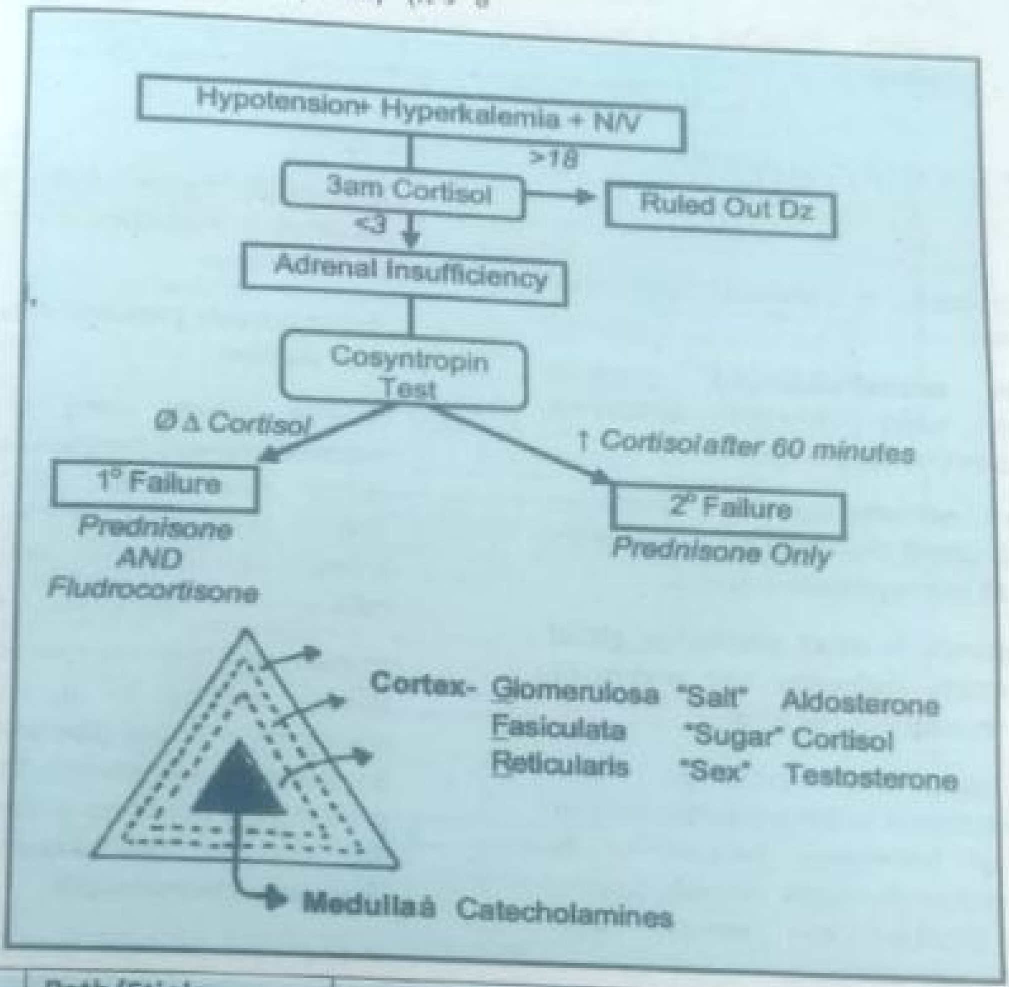
It's ok to **watch and wait** if **<4cm**, but intervene with treatment if **>4cm** or there's an **increase** in **size over time.**

r/o...	With
Cushing's	Dexamethasone Suppression test
Pheo	24-Hr urine
Conn's	Aldo/Renin

Adrenal Insufficiency

- The loss of adrenal function may be from a variety of **etiologies,** and may be sudden/acute with multiple **presentations.**
- The **most common cause** in the US is **autoimmune adrenalitis;** it's **TB worldwide.**
- In the setting of **sepsis** there may be bilateral adrenal destruction from **hemorrhage (Waterhouse-Friderichsen).**
- Weird **deposition disease** can also compromise the adrenals (amyloid, sarcoid, and hemochromatosis).
- In **primary failure** (loss of cortisol, maintenance of ACTH) the symptoms will be **hypotension, fatigue, N/V** of cortisol loss, as well as the **hyperpigmentation and hyperkalemia.**
- Hyperpigmentation is a result of ACTH production trying to increase cortisol while hyperkalemia is from deficient aldosterone.
- In **secondary failure,** no ACTH is produced so hyperpigmentation is absent. Because aldosterone production is intact there's also no hyperkalemia. It's key to make sure it's not a primary deficiency so perform a **cosyntropin test** (exogenous ACTH administration).
- Establish a baseline cortisol in the morning (**<3ug = Dz, >18ug = ruled out**).
- Give the ACTH then reassess in 60 minutes to determine if there's any change in cortisol. **(3, 3, 3** = **Ø** ACTH **problem** = **1° deficiency)** vs **(3, 3, 20** = ACTH **problem, 2° deficiency).**

- Treat this by **giving the steroids** they don't have.
- **Prednisone** for all types and **fludrocortisone** for primary only (it's a synthetic aldo that has its function retained through the RAAS in secondary).


Hypotension+ Hyperkalemia + N/V
>18
3am Cortisol
Ruled Out Dz
<3
Adrenal Insufficiency
Cosyntropin Test
Ø Δ Cortisol
↑ Cortisol after 60 minutes
1° Failure
Prednisone AND Fludrocortisone
2° Failure
Prednisone Only
Cortex- Glomerulosa "Salt" Aldosterone
Fasiculata "Sugar" Cortisol
Reticularis "Sex" Testosterone
Medullaà Catecholamines

Dz	Path/Etiology	Presentation	Diagnostic	Tx
Cushing's	Iatrogenic Pituitary Tumor Adrenal Tumor Ectopic Tumor	Obesity, Diabetes Moon Facies, Buffalo Hump	Low Dose Dexa Suppression ACTH levels High Dose Dexa Suppression CT/MRI Abd/Pelvis/Thorax	Stop Steroids or Cut out Tumor
Hyperaldo (Conn's)	1o Dz = Tumor 2o Dz = Systemic Mimickers	Hypertension and HypoK OR Refractory HTN	Aldo, Renin, Aldo:Renin Salt Suppression CT/MRI MIBG Scintillography	Cut out Tumor Fix Systemic Dz
Pheo	Adrenal Tumor	Paroxysmal Pain Pressure Palpitations Pallor Perspiration	24-hr Urinary Metanephrine Or VMA Urine CT/MRI	α-Blockade β-Blockade Adrenalectomy

Adrenal Insufficiency	Autoimmune Infection Hemorrhage Deposition Disease Pituitary Failure	Hypotension Fatigue Anorexia Nausea/Vomiting Hyperpigmentation	Cortisol Level @ 3am Cosyntropin Test CT/MRI	1o = Prednisone (cortisol) and Fludrocortisone 2o = Prednisone Only

ANTERIORPITUITARY

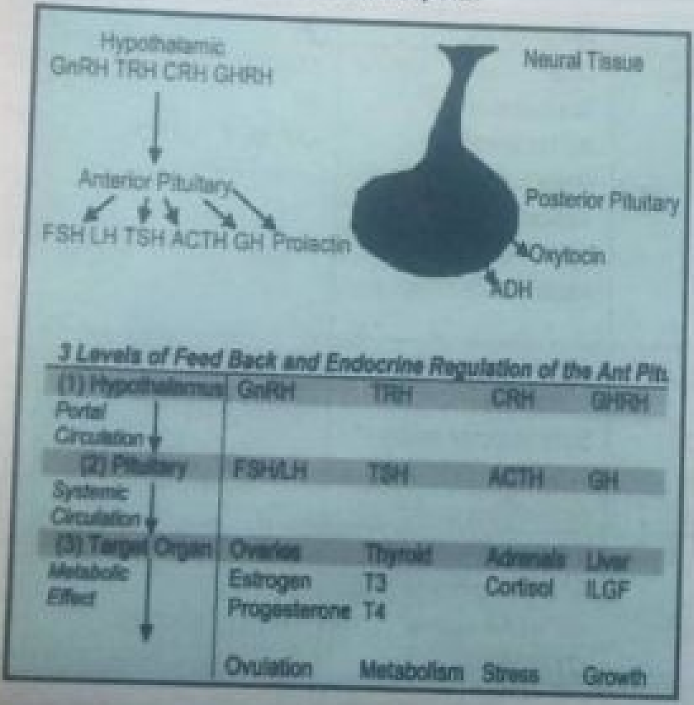
Anatomy

- The pituitary is divided into two structures:

  1) the **adenohypophysis** (anterior pituitary), which receives **endocrine** signals from the hypothalamus.

  2) the **neurohypophysis** (posterior pituitary), which has axon terminals from neurons of the hypothalamus in it.

- The pituitary's a **small endocrine gland** that regulates **endocrine** and **metabolic function** throughout the body.
- There can be problems with overproduction or underproduction of just one or all hormones. Because of its location within the **optic chiasm**, tumors of the pituitary can present with **bitemporal hemianopsia**.



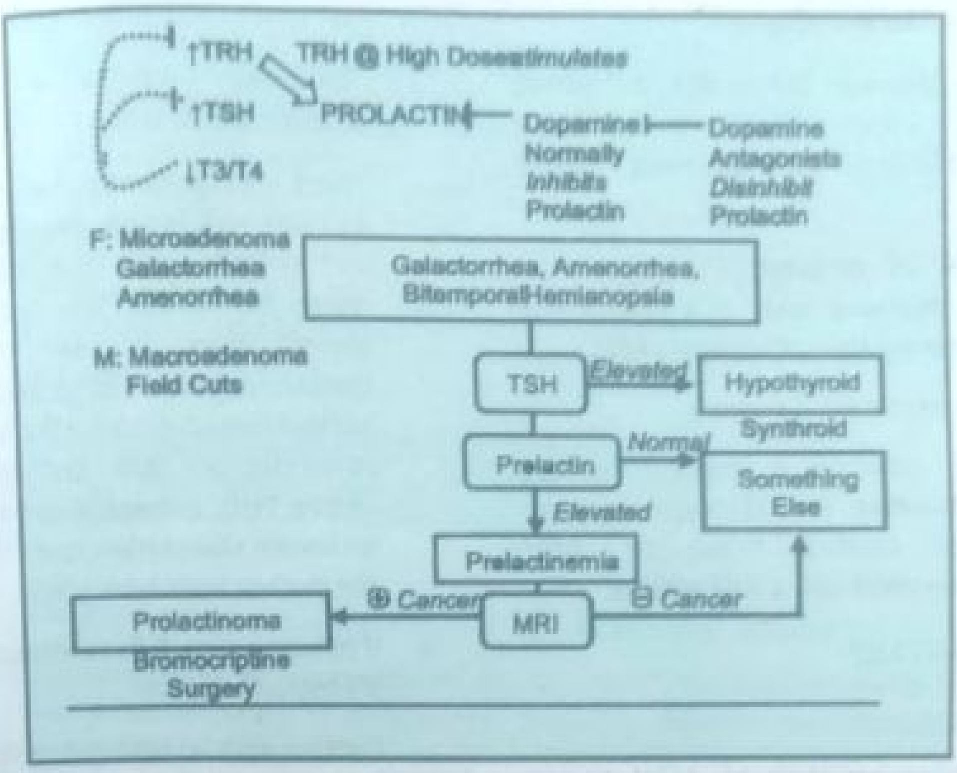
3 Levels of Feed Back and Endocrine Regulation of the Ant Pit.

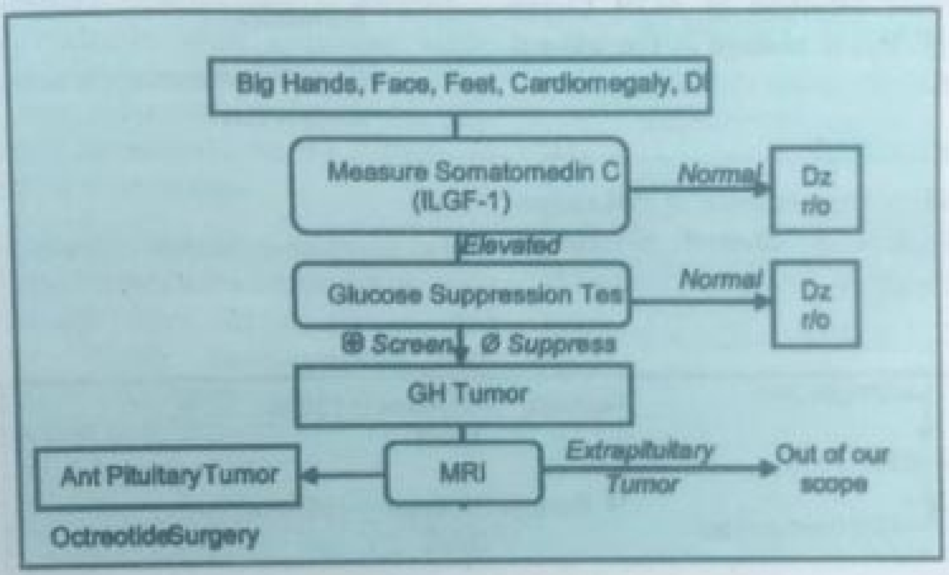
(1) Hypothalamus	GnRH	TRH	CRH	GHRH
Portal Circulation				
(2) Pituitary	FSH/LH	TSH	ACTH	GH
Systemic Circulation				
(3) Target Organ	Ovaries	Thyroid	Adrenals	Liver
Metabolic Effect	Estrogen Progesterone	T3 T4	Cortisol	ILGF
	Ovulation	Metabolism	Stress	Growth

1) Prolactinoma

- A benign tumor that **autonomously secretes Prolactin** will cause a prolactinemia.
- Prolactinemia presents differently in men than women.
- They're caught early in women as **microadenomas**, because women tend to notice **galactorrhea** and **amenorrhea**. There's been no time for the tumor to grow; it's small and presents **without field cuts**.
- In **men**, who don't lactate or have periods, there's nothing to tip them off that something's wrong **(decreased libido may be the only symptom)**. Thus, the tumor grows. As it becomes a **macroadenoma** it digs into the **optic chiasm** to produce a **bitemporal hemianopia**.
- In the case of field cuts it's easy to be pretty sure there's a tumor.
- But in the case of a microadenoma other causes of prolactinemia must be ruled out. For example, **dopamine antagonists** (antipsychotics) disinhibit Prolactin while **↑↑TRH** (from **hypothyroidism**) stimulates its production.
- So, before getting an **MRI** test, get **Prolactin levels** and a **TSH** after looking over their med list.
- Treat by using **dopamine agonists (cabergoline > bromocriptine).**
- Consider surgery only after medical therapy fails; unlike most tumors.
- Prolactinomas are very sensitive to medical therapy.

- Follow prolactinomas with prolactin levels q3months and an MRI annually until stable.


↑TRH
TRH @ High Dosestimulates
↑TSH
PROLACTIN
Dopamine Normally *Inhibits* Prolactin
Dopamine Antagonists *Disinhibit* Prolactin
↓T3/T4
F: Microadenoma Galactorrhea Amenorrhea
M: Macroadenoma Field Cuts
Galactorrhea, Amenorrhea, BitemporalHemianopsia
TSH
Elevated
Hypothyroid
Synthroid
Prolactin
Normal
Something Else
Elevated
Prolactinemia
⊕ *Cancer*
MRI
⊖ *Cancer*
Prolactinoma
Bromocriptine Surgery


Big Hands, Face, Feet, Cardiomegaly, DI
Measure Somatomedin C (ILGF-1)
Normal
Dz r/o
Elevated
Glucose Suppression Tes
Normal
Dz r/o
⊕ *Screen*
Ø *Suppress*
GH Tumor
MRI
Extrapituitary Tumor
Out of our scope
Ant PituitaryTumor
OctreotideSurgery

2) Acromegaly

- A benign tumor that **autonomously secretes Growth Hormone** will cause things that can grow to grow.
- In a **child**, before the closure of the growth plates, that means the long bones – resulting in **gigantism**.
- But in an **adult** it means the **hands**, **feet**, **face**, and **visceral organs**.
- It also induces **gluconeogenesis** and causes the patient to present with **glucose intolerance** or even **frank diabetes**.
- The thing that kills these patients is the **cardiomegaly** and subsequent diastolic heart failure.

- The diagnosis is made biochemically.
- However, GH is pulsatile, and so it **can't be used to make the diagnosis**.
- Instead, because GH exacts its effects through the liver via **ILGF-1** (somatomedin); the diagnosis begins there.
- A **failure to suppress** GH levels in a **glucose tolerance test** is a finding and should prompt the confirmatory **MRI**.
- The only treatment is **surgery**.
- However, radiation or medical therapy with **octreotide** (somatostatin) can be used for residual tissue to ↓GH production which will ↓ILGF effects.

ANTERIOR PITUITARY

3) Cushing's Disease

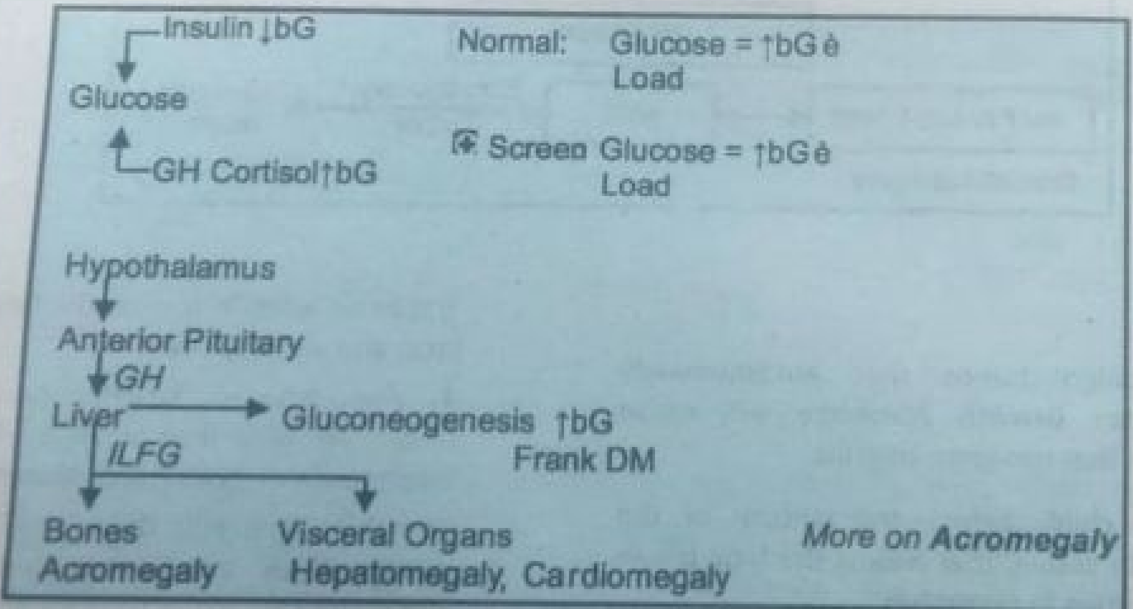
- Autonomous secretion of **ACTH** causes **↑cortisol.** This is covered in the adrenal disorders.

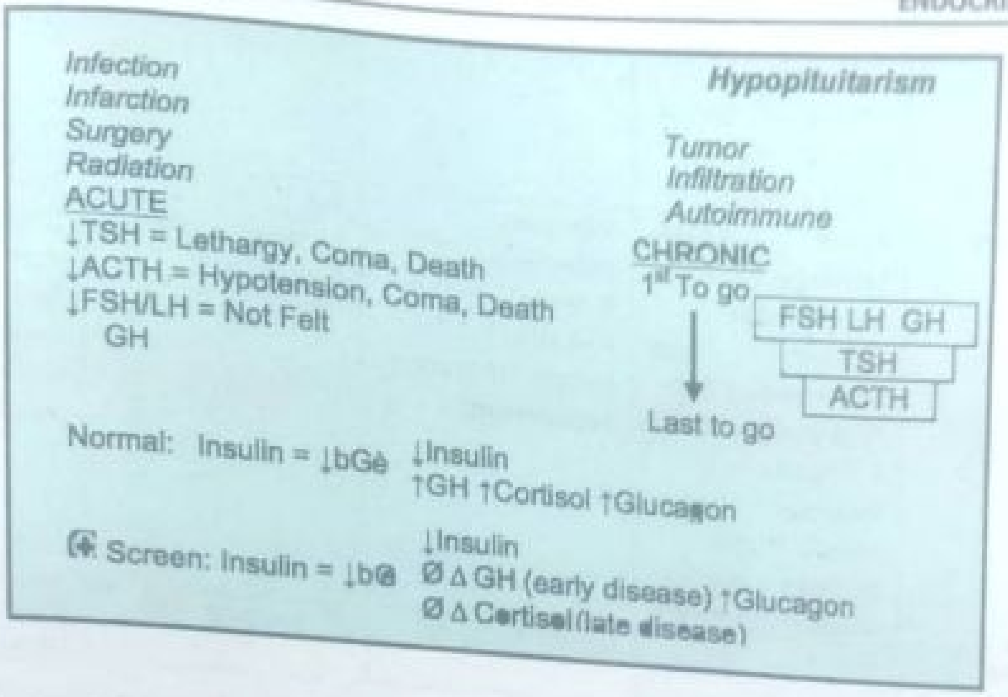
4) Central Hyperthyroidism

- An incredibly rare secretion of **TSH** causes **↑T4/T3**. This is covered in thyroid disorders.

5) Hypopituitarism

- The lack of one or all pituitary hormones can cause some problems for the body.
- There are a variety of ways pituitary function can be lost.
- There are acute losses that usually present as really sick (**coma, hypotension, death**) and **chronic** losses that result in losing lesser hormones first. Let's start with **chronic** then go over some specific syndromes that need to be known about acute diseases. Because the less important hormones are lost first (FSH and GH before TSH), **screening** can be done with an **insulin stimulation test** - the reverse of the glucose suppression test.
- If hypoglycemia **fails to stimulate** GH then it's hypopituitarism.
- Confirm with an **MRI** and **replace deficient hormones**.
- If possible, reverse the underlying cause if there is one.


Insulin ↓bG
Glucose
GH Cortisol ↑bG
Normal: Glucose = ↑bG è Load
Screen Glucose = ↑bG è Load
Hypothalamus
Anterior Pituitary
GH
Liver
Gluconeogenesis ↑bG
Frank DM
ILFG
Bones
Acromegaly
Visceral Organs
Hepatomegaly, Cardiomegaly
More on Acromegaly



Hypopituitarism

Infection
Infarction
Surgery
Radiation
ACUTE
↓TSH = Lethargy, Coma, Death
↓ACTH = Hypotension, Coma, Death
↓FSH/LH = Not Felt
GH

Tumor
Infiltration
Autoimmune
CHRONIC
1st To go
FSH LH GH
TSH
ACTH
Last to go

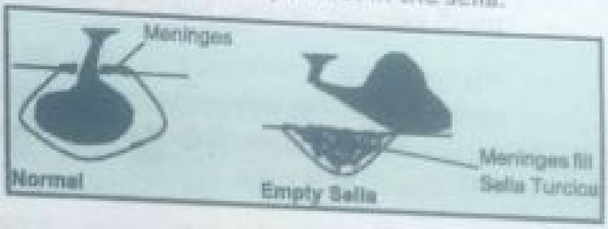
Normal: Insulin = ↓bGè ↓Insulin
↑GH ↑Cortisol ↑Glucagon

⊕ Screen: Insulin = ↓b@ ↓Insulin
Ø Δ GH (early disease) ↑Glucagon
Ø Δ Cortisol (late disease)

- Acute loss of function is much worse.
- Specific syndromes to be aware of are Sheehan's and Apoplexy.
- **Sheehan's** is a postpartum hypopituitarism after prolonged labor, usually with some blood loss. The pituitary becomes ischemic and dies. This can typically be detected by the inability to lactate as the first sign.
- **Apoplexy** is a medical emergency; a pre-existing pituitary tumor outgrows its blood supply and bleeds into the pituitary. The patient rapidly decompensates with stupor, nuchal rigidity, headache, nausea and vomiting, etc.

6) Empty Sella Syndrome

- This is an **incidental finding** in a patient who has **no endocrine abnormalities** but is found to have an "absent pituitary" on an **MRI** they had for some other reason.
- If it ain't broke, don't fix it. They have a pituitary – it's just not in the sella.



	Patient Presentation	Pathology	Dx	Tx
Prolactinoma	F: Amenorrhea, Galactorrhea, Ø Vision Δs, Microadenoma M: Vision Δs, Macroadenoma	Dopamine Antagonists Hypothyroid Pituitary Tumor ↑Prolactin	1st: Prolactin Then: TSH/T4 Best: MRI	Start: Bromocriptine Best: Surgery when pregnancy, field cuts, medication failure
Acromegaly	**Acromegaly** Children:	↑GH	1st: Glucose Suppression Test	Start: Octreotide Best: Surgery

	Gigantism Adults: Big hands, Big Feet, Big Heart and DM		Best: MRI	
Hypopituitary Sheehan's Apoplexy	Acute: Coma, Lethargy, Hypotension Chronic: Less important go first Post-partum after a long labor Previous Tumor Bleeds, Stupor Nuchal Rigidity, Nausea/Vomiting	Infection, Infarction, Surgery, Radiation, Tumor, Infiltration, Autoimmune	1st: Glucose Stimulation Test Best: MRI	Start: Replace Missing Hormones Best: Treat underlying disease if possible
Empty Sella Syndrome	Anx	Not pathological	1st and Best: MRI	Ø: Needs no treatment

DIABETIC EMERGENCIES

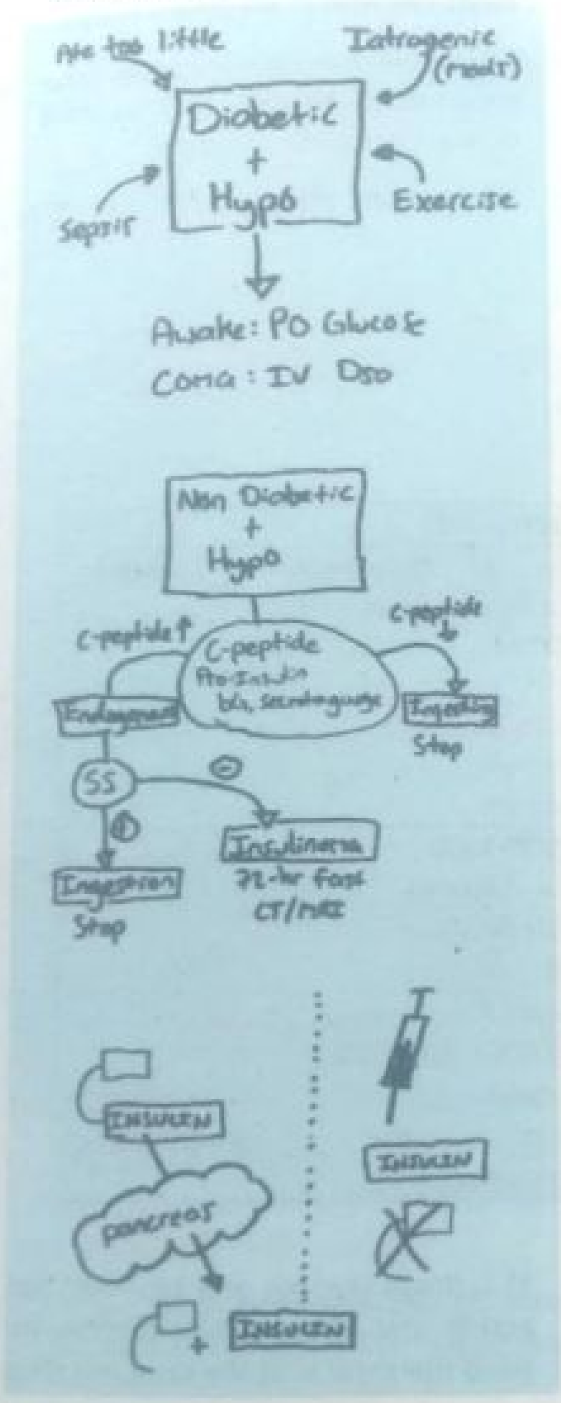
Hypoglycemia in a Diabetic

- Hypoglycemia in a diabetic can come from a number of causes.
- The usual suspects are **too little food, too much exercise**, and **too much medication**.
- Hypoglycemia is defined as a **bG < 70** or **symptoms of hypoglycemia** (palpitations, perspiration, presyncope); it's corrected with ingestion of sugar.
- Severe hypoglycemia may cause coma, anoxic brain injury, and death.
- The **most important thing** to do is get the sugar up. Do it with an **oral glucose load** if the patient is awake, or with **IV D50** if the patient is in a coma.
- After the event has resolved, assess life-style and medications to determine exactly what happened and try to prevent it in the future.
- Hypoglycemic events are potentially fatal and should be treated with significantly more acuity than a high reading.

Hypoglycemia in a Non-Diabetic

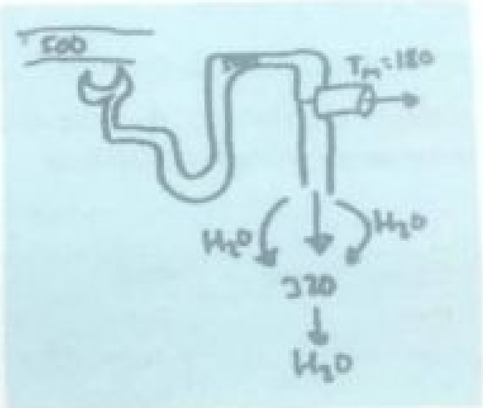
- Hypoglycemia, a **bG < 60** AND **symptoms**, in a non-diabetic is usually factitious disorder.
- Two potential disease states (that are quite rare) are **insulinoma** and **autoimmune hypoglycemia**.
- To discover if the patient is doing it to themselves, obtain a **C-peptide**, **Pro-Insulin, bG,** and **Secretagogue screen.**
- Endogenous insulin comes from Pro-insulin, cleaving the C-peptide portion to result in insulin. Thus, if there's **NO rise in C-peptide**, the insulin must be exogenous (**self-injecting**). Your job is done if the C-peptide is normal.
- Endogenous insulin secretion may be **induced by secretagogues** (like sulfonylureas) or **produced by insulinomas**. The only way to tell the two apart is to obtain a **secretagogue screen**. If **positive,** they're ingesting secretagogues - tell them to stop.
- Only evaluate for insulinoma if the **C-peptide is elevated** AND the **secretagogue screen is negative**.

- Perform a 72-hour fast, retest for all the same things above, and if positive perform the CT scan or MRI of the abdomen to find + resect the tumor.
- If all else fails, consider the option of looking at **insulin antibodies**.


Ate too little
Iatrogenic (meds)
Diabetic + Hypo
Sepsis
Exercise
Awake: PO Glucose
Coma: IV D50
Non Diabetic + Hypo
C-peptide ↑
C-peptide ↓
C-peptide
Pro-Insulin
bG, secretagogue
Endogenous
Ingestion
Stop
SS
⊖
⊕
Insulinoma
72-hr fast
CT/MRI
Ingestion
Stop
INSULIN
pancreas
INSULIN
INSULIN
+

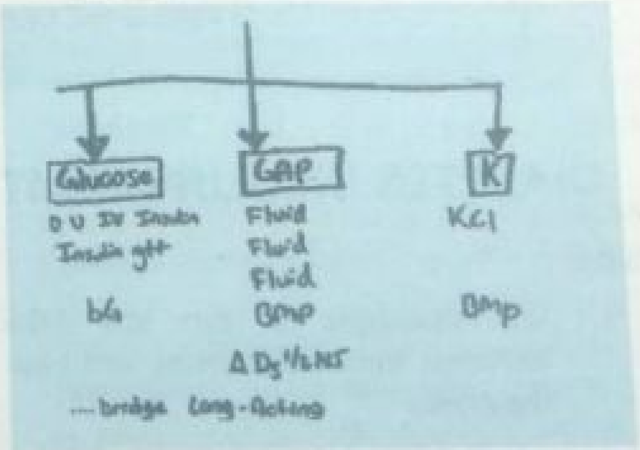
Diabetic Ketoacidosis

- DKA is a life-threatening emergency of Type I diabetics.
- There is plenty of sugar in the blood, but without insulin none of it can get into the cells.
- It's as if the patient is starving. The brain activates **ketones** from fatty acids, causing both **ketosis** and **acidosis**.
- Simultaneously, the high levels of sugar in the blood spill into the urine. With the Tmax of the renal tubules at only about 180, excess glucose is spilled into the urine. Glucose is a potent osmotic diuretic; the patient becomes dehydrated.


500
Tm=180
H2O
H2O
320
H2O

Mechanism of dehydration in hyperglycemia. Excess glucose is lost in urine and draws with it water, leading to potent diuresis.

- The patient will present **obtunded** or **in a coma**. They will be dry.
- Diagnose the condition by finding **elevation blood glucose** (Diabetic) **ketones in the urine and blood** (Keto) and **acidosis on ABG / anion gap on BMP** (Acidosis).


Glucose
GAP
K
0 U IV Insulin
Insulin gtt
Fluid
Fluid
Fluid
KCl
bG
BMP
BMP
Δ D5 1/2 NS
...bridge Long-Acting

Treatment of DKA. Replete K, give insulin, then give fluids. HHS/HHNKC is the same thing, except no need to follow anion gap.

- The treatment is ***threefold:*** **Replete Potassium** before giving Insulin, **IV Insulin**, and **Fluid**. Monitor therapy with hourly blood glucoses and BMPs every 4 hours. If the **gap hasn't closed** but the **glucose is approaching normal** (this value differs per protocol) switch to **D5 ½ NS.** As the anion gap resolves ("the gap closes") bridge to **subQ insulin** long acting and let them eat.
- While insulin noncompliance is the most common cause of DKA, also look for NSTEMI, GI bleeds, and infections as precipitating causes.

Hyperosmolar Hyperglycemic Non-ketotic Coma

- HHNKC or HHS is the ***life-threatening emergency of Type II diabetics.***
- **No ketones** are made because there's sufficient insulin to feed the brain.
- **No acidosis** occurs because fatty acids aren't accessed.
- However, the patient will still present with **coma** because of **profound dehydration**.
- The blood glucoses are often much more **elevated in HHNKC** than in **DKA** + the diuresis has gone on longer.
- This patient needs **fluids and IV Insulin**

Characteristic	**DKA**	**HHNKC/ HHS**
Path:	**Type I,** Insulin Dependent Diabetes Mellitus (IDDM)	**Type II,** Non-Insulin Dependent Diabetes Mellitus (NIDDM)
Pt:	+ Diabetic Coma + Ketones + Acidosis	+ Diabetic Coma - Ketones - Acidosis
Dx:	**bG 300-500** U/A: + Ketones ABG: + Acidosis BMP: + Gap	**bG 800-1000** U/A: - Ketones ABG: - Acidosis BMP: - Gap
Tx:	Replete K IV Fluids – Bolus a lot IV insulin **Follow the GAP**	Replete K IV Fluids – Bolus a lot IV Insulin Follow the symptomatic improvement

DIABETES INSULIN MGMT

Insulins

- It's imperative to learn the difference between their **peak onset** and how long **they last.**
- All insulins require **SubQ injections**. Some hints to help get started.

1) L drugs (**L**antus and **L**evemir) are **Long acting** and all equivocal (except for how good the meal is at the drug rep dinner).

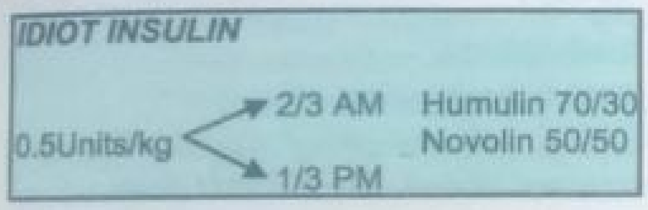
2) Log math is more advanced than drawing a **Line**, so **Log** drugs (Humalog Novolog) are used in more complex ways (qAc) versus the

3) **Lin** drugs (Humu**Lin** Novo**Lin**), which as we'll see are ancient, not great, and useful for those who don't want to think.

Finally, 4) NPH is the **rapid** part of the log combos, while

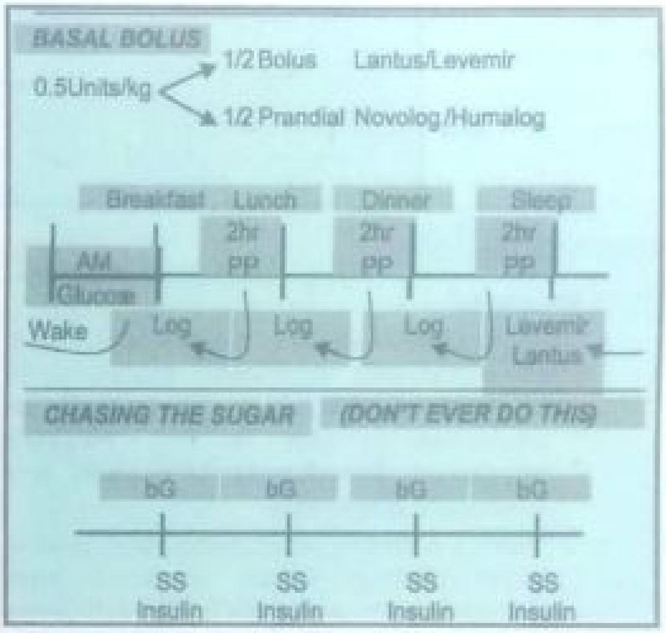
5) **regular** insulin is a longer acting (medium) insulin.

Lantus Levemir	Long Acting Insulin	Basal Insulin	qPM
HumaLog **NovoLog**	**Rapid acting** **Insulin Combo**	Prandial Insulin	qAC
HumuLin **NovoLin**	**Medium acting Insulin Combo (old school, easy)**	Idiot Insulin	biD
NPH	**Rapid Actin**	Prandial	qAC
Regular	**Rapid Acting**	Generally useless	


IDIOT INSULIN
0.5Units/kg
2/3 AM
1/3 PM
Humulin 70/30
Novolin 50/50

Insulin Regimen

- The goal of insulin regimens is to control the blood glucose as though it were a normal pancreas.
- That means **post prandial glucose spikes** are met by **insulin spikes post-prandially.**
- There is also a certain level of insulin always floating around in the body – it's called **basal insulin**. So to simulate a normal pancreas the **basal-bolus** is **best**.
- Insulin demand can be approximated by **0.5 Units/kilogram** the total amount per day.
- In the basal bolus method, ½ is in the **night time** as **Long Acting Insulin** (the basal).
- The other ½ is divided **qAC** of **short acting** insulin (the bolus).
- It's important to remember that a blood sugar is affected by the **insulin that precedes it**.
- If the **AM Dose** is high, increase the nighttime dose. If the bG taken near lunch is high, increase the breakfast dose.


BASAL BOLUS
0.5Units/kg
1/2 Bolus
Lantus/Levemir
1/2 Prandial
Novolog/Humalog
Breakfast
Lunch
Dinner
Sleep
2hr PP
2hr PP
2hr PP
AM Glucose
Wake
Log
Log
Log
Levemir Lantus
CHASING THE SUGAR
(DON'T EVER DO THIS)
bG
bG
bG
bG
SS Insulin
SS Insulin
SS Insulin
SS Insulin

- A lot of people try the **Idiot Insulin** method. It's called (I call it) idiot insulin because the **same amount** of **medium acting insulin** is given regardless of the blood sugar. If patients don't want to **check bG or are afraid of needles,** they can use this method. It has **poor basal coverage** and **poor post prandial coverage,** but it's only **BID dosing.**
- The **worst** method is **sliding scale insulin** where **no basal insulin** is given.
- Rather, a certain amount of **short-acting insulin** is given with each accu-check. **Bad hospitalists** will do this. Since current bG is a product of the last insulin it will create **hyperglycemic peaks** and **hypoglycemic troughs** as the nurse tries to chase down the bG on your orders.

- If following another regimen and sugars are still high, adjustment of daily doses is appropriate.
- However, if the patient eats a **cake** or has **ridiculous bG** one time, using the sliding scale is a great supplement - but only **on top of** an existing regimen.

Effect	Findings
Somogyi Effect	Too MUCH insulin at night → High AM bG
Dawn Phenomena	Too LITTLE insulin at night → High AM bG
Check early AM bG to tell the difference	

Complications	*What we do*
CAD or HF	ACE-i
Nephropathy	Microalbumin Screen, ACE-i
Peripheral Neuropathy	Foot care, education, educations
Eyes	Fundoscopic Exams, Laser
Erectile Dysfunction	Nighttime Tumescence, Viagra
Control the Blood Sugars is paramount	

MEN SYNDROMES

MEN1 Syndrome

- Also known as **Wermer's Syndrome,** this is an **autosomal dominant** mutation of **MEN1 gene** that causes hyperplasia or adenomas of the **"3 Ps:" Pituitary Adenomas, Parathyroid Adenomas,** and **Pancreatic Adenomas**.
- There's a strong association with Gastric Ulcers (Zollinger-Ellison syndrome from the pancreatic adenomas), Hypoglycemia (Insulinoma), and Hypercalcemia (PTH).

MEN2A and MEN2B

- These are essentially the same disease and aren't clearly separated.
- Both are caused by a mutation in the **RET proto-oncogene**.
- They cause endocrine tumors everywhere except the 3ps.

MEN1 = Pituitary + Pancreas + Parathyroid
MEN2A = Pheochromocytomas + Thyroid + Parathyroid
MEN2B = Pheochromocytomas + Thyroid + Neuronal

- Look for **Pheochromocytomas** and **thyroid adenomas.**
- The parathyroid gland can also be involved, but isn't classic. Really, the only difference between **2A and 2B** is the presence of **neuronal tumors** found in MEN2B.

Real life vs test

- This is rare (~1 in 50,000) – you're not going to see it.
- If there's a combination of:

- recurrent endocrine neoplasias +
- age <40 +
- family history +
- multiple organ systems affected

You'd suspect something was up and do a **mutational analysis** of the **MEN1/2 genes.**

OUTPATIENT DIABETES

Diagnosing Diabetes

- Screening is indicated when there are risk factors such as an **elevated** BMI, **hypertension, or advanced age.**
- Different screening tools exist, each with their own advantages.
- The **random glucose** is convenient – it can be obtained at any time without preparation and it's a one-time test.
- The diagnosis is made if the random glucose is **> 200** and there **are symptoms** of diabetes (polyuria, polydipsia).

- **No repeat confirmatory test** is necessary. The random glucose can be affected by **acute stress, such as illness or steroid use, and does not reflect the long-term impact on the body.**
- The **fasting glucose** is a better screen but requires preparation. The patient must have an **overnight fast.** It also needs a **second confirmatory check**. A **bG > 125** on the fasting check is indicative of diabetes.
- **< 100** is normal and **between 100-125** is termed prediabetes or insulin insensitivity.
- The **oral glucose tolerance test** accurately reflects the pathophysiology of diabetes but is time-intensive.
- The patient has a fasting check, then consumes an oral glucose load **of 75g.**
- Two hours later the glucose is tested (effectively the post-prandial glucose).
- A value of **< 140 is normal, 140-199 is prediabetes,** and **> 200** is **diabetes.**
- The **HgbA1c** is the preferred method in the United States because it **reflects the past 3 months of blood glucose** and is a more accurate reflection of what's happened rather than what's going on in the body immediately (it isn't influenced by stress or infection like a one-time glucose check is).
- However, it may miss early glucose abnormalities and requires ***3 months of hyperglycemia to turn positive (thus it's NOT used to screen for gestational diabetes).***
- **A normal A1c** is **< 5.7**. **Prediabetes** is between **5.7 and 6.4**, and **diabetes A1c** is **> 6.5**.
- When considering **Type I diabetes** ***(even if the onset is in adult age ranges)*** measurement of **autoantibodies** are recommended. If the patient has ***rapidly progressive diabetes refractory to oral medications or has a high insulin requirement*** despite being relatively normal weight, assess **GAD65** and **IA-2** antibodies.
  - Those who have **slowly progressive type II diabetes** shouldn't have antibodies checked.
  - **"Type I"** should be considered instead **"autoimmune destruction"** and can occur **at any age or BMI range.**

Treating Pre-diabetes

- Early intervention can delay or prevent the onset of diabetes. When in the pre-diabetic range **metformin** and **lifestyle adjustment** (diet and exercise) are absolutely indicated and can prevent diabetes onset.

Screening and Diagnosing Diabetes

Random Glucose

Normal < 200

Diabetes> 200

Must have symptoms of diabetes

Fasting Glucose

Normal < 100

Prediabetes 100-124

Diabetes> 125

Must have two readings to confirm

2-Hour Glucose Tolerance Test

Normal < 140

Prediabetes 140-199

Diabetes> 200

Indicated when prediabetes is found on fasting

A1c

Normal < 5.7

Prediabetes 5.7-6.4

Diabetes> 6.5

May miss early disease, do not use in gestational

Type 1 – Autoimmune Destruction

Usual	Juvenile Onset Type I Diabetes Type I Physiology, Antibodies Positive Childhood
LADA	Late Autoimmune Diabetes in Adults Type I Physiology, Antibodies Positive Adult Age
Idiopathic	Type I just because (rare) Type I Physiology, Antibodies negative Adult Age

Treatment of Pre-Diabetes

Diet and Exercise Metformin	(Start both at the same time)

Treatment of Type I Diabetes

- Type I diabetics will require **life-long insulin therapy**.
- If they can maintain adequate glycemic control on ***multiple injections per day therapy,*** they should continue that.
- If they can't, they should be considered for **insulin pumps** and/or **continuous monitor glucose** devices.

Treatment of Diabetes – Non Insulins

Lifestyle is always the first step.

- **Metformin** is the by far the best pharmacologic therapy and is **always first line** unless contraindicated. Metformin can't be used in **CKD, CHF, or liver disease** because of the risk of ***lactic acidosis***. It should **always be held** when hospitalized.
- The **second-line agent** is chosen based on patient preference and side effect profile.
- The combination of **three of more oral agents** is **NOT SUPERIOR** compared to **two agents.** Failure of two oral agents should prompt insulin.
- In general, initiation of lifestyle modifications can reduce the A1c by about 1%.
- Oral agents reduce the A1c by 3%.
- If the patient has an A1c >9%, insulin should be started.

Type	Name	Mechanism	SE
Giguanides	Metformin	↑Insulin sensitivity	Diarrhea
Sulfonylurea	Glyburdie Glipizide	↑Insulin secretion	Hypoglycemia
TZDs	Pioglitazone	↑Insulin Sensitivity	Weight Gain
DDP-4-I (liptins)	Sitagliptin Saxagliptin	DDP-4-i	Weight Neutral
GLP-1 analogs	Exenatide Liraglutide	↑GLP-1	Weight Loss
Meglitinides	Repaglinide Nateglinide	↑Insulin Secretion	Hypoglycemia
SGLT2-i	Canagliflozin Dapagliflozin	Block glucose absorption in kidneys	Euglycemic DKA
Alpha-Glucosidase Inhibitors	Acarbose Miglitol	Block intestinal Absorption	Diarrhea, Gas

Ongoing Assessment of Diabetes

- **Self-monitoring** of blood sugar is a means of controlling blood glucose for those with insulin.
- **Pre-prandial** glucose checks are used for all-comers.
- Once the pre-prandial glucoses are at goal but the A1c is not, **post-prandial** glucose checks can be added.
- Those patients who do NOT use insulin should NOT use self-monitoring of blood glucose.
- The **A1c** is assessed every **three months** for all patients with prediabetes, diabetes, and insulin-dependent diabetes.
- The goal **A1c is <7.**

Do What	When
Self-Monitoring of Blood Glucose	On insulin
Pre-Prandial Checks	On insulin
Post-Prandial Checks	Pre-prandials are controlled by A1c is not
A1c	Every 3 monhts

Preventative Care in Diabetes

- Diabetes takes the **eyes,** the **kidneys, and the nerves.**
- Longstanding diabetes and the microvascular changes it brings can lead to **amputations, blindness, and dialysis.**
- **Diabetic wounds** are difficult to heal due to the microvascular damage.
- Diabetic wounds form because of the peripheral neuropathy that develops. So, screening becomes important.
- A **physician** needs to screen for **retinopathy every year** with a retinal examination, **nephropathy every year** with a ***urinalysis and microalbumin/creatinine ratio,*** and **neuropathy every year** with a monofilament wire examination.
- Patients should be educated to exam their feet periodically for wounds and to ensure that shoes are not too tight.

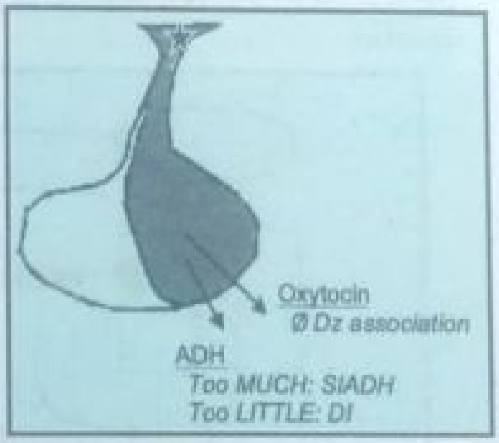
Complication	*Screen*	*Treatment*
Retinopathy	Retina Exam	Laser
Nephrophathy	Microalb/Crea	Ace-inhibitor
Neuropathy	Monofilament	Gabapentin

POSTERIOR PITUITARY

Introduction

- The **posterior pituitary** is actually an extension of the hypothalamus.
- Neurons of the hypothalamus produce **oxytocin** and **ADH**, where they are transported to the posterior pituitary for storage.
- **Deficiency in or excess of Oxytocin** causes no disease.
- **ADH** on the other hand has **two potential diseases.**

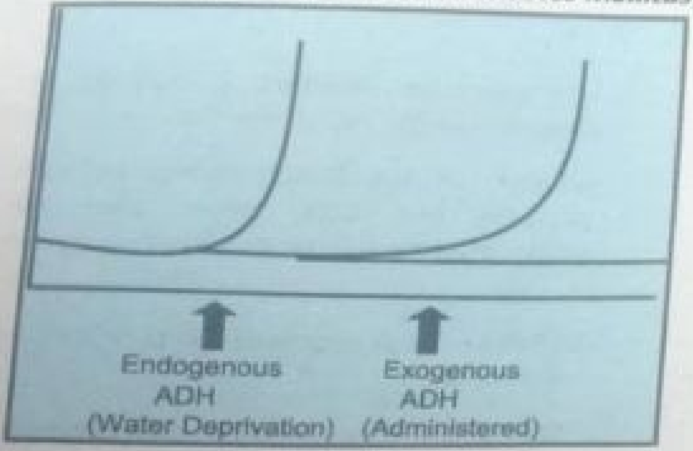
  ↑ADH = SIADH = Hypo Na from too much water being retained. **↓ADH = DI = HyperNa** from too much water lost.
- Any **acute** or **chronic** process can disrupt the stalk or neuronal processing, leading to either condition.



1) Diabetes Insipidus

- A patient **deficient in ADH** the kidneys has no signal to retain water so they will pee a lot. This leads to them ***getting thirsty and drinking a lot***. Thus the patient with DI will present with **polydipsia** and **polyuria**. Sounds like regular diabetes.

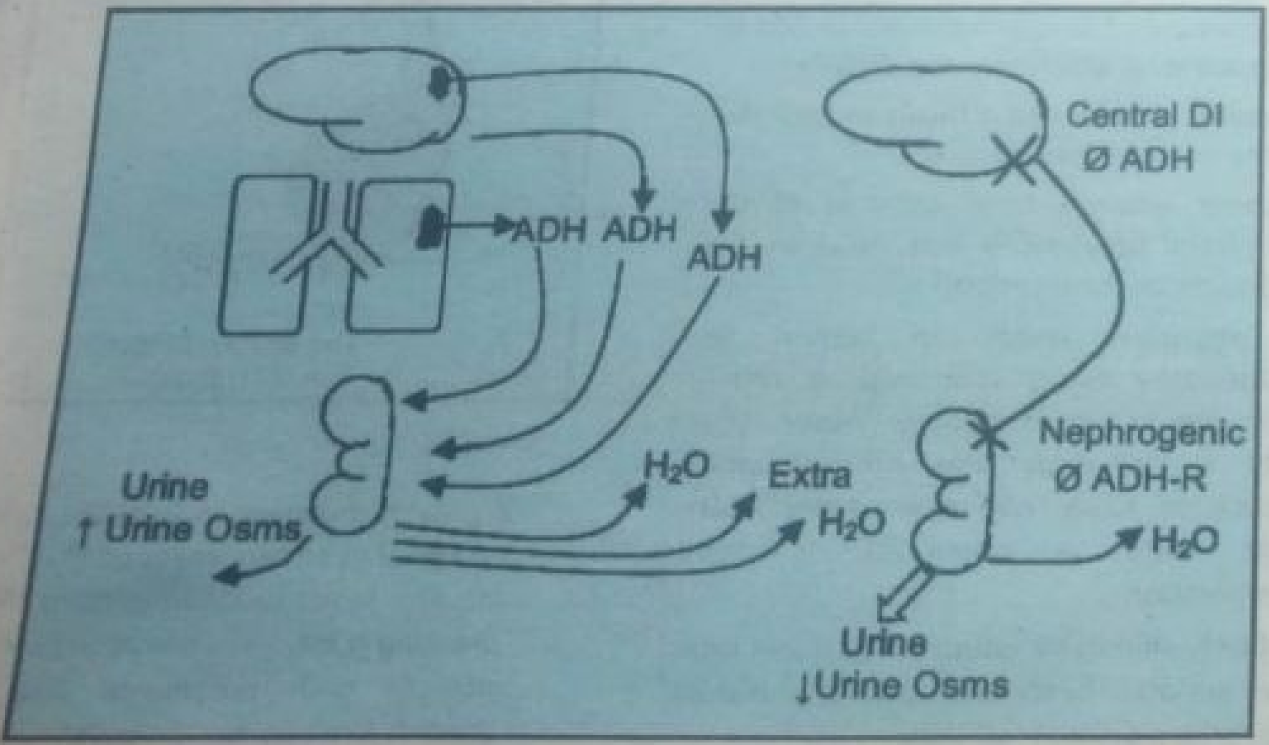
- *The difference is in the urine;* **DM** has **hypertonic urine** full of **glucose** pulling water with it. **DI** has **hypotonic urine** because even though the patient is becoming dehydrated, the kidneys can't retain the water.
- Thus, the **first test to get** is a **U/A** looking for **glucose** ***(to rule out diabetes mellitus)***.



- If negative the decision's between **Nephrogenic** (+ ADH but broken receptors) and **Central** (kidneys work fine - there's just ØADH being made).
- Do that with a **water deprivation test** .
- Treat psychogenic polydipsia with psychotherapy, **central diabetes** with **desmopressin,** and **Nephrogenic DI** with **diuretics.**
- Obviously, start with hydration with IVF to correct electrolyte abnormalities.

2) Syndrome of Inappropriate ADH

- When there's **too much ADH** the kidneys absorb all the water there is, leaving behind a urine rich in Na.
- The patient **dilutes their blood** (hyponatremia and hypotonic serum) and **concentrates their urine** - the opposite of DI. The ADH came from the **brain** (tumor, infection, trauma, or granuloma) or the **lungs** (TB, COPD, and Cancer).
- However, **hypothyroid** can do it as well as **TSH simulates ADH** at high doses.
- The patient will present with **hyponatremia**.
- Get a **serum Osms** (low) and **Urine Osms** (high).
- The goal should be to **treat the underlying disease**.
- In the meantime, induce a Nephrogenic DI with **Demeclocycline** to get rid of the free water.
- If HypoNa is severe, replace with hypertonic saline.



Dz	Pt	U/A	Water *Deprivation Test*	Tx	Cause
Diabetes Mellitus	Polydipsia Polyunia Weight Loss	Hypertonic Urine with Glucose	N/A	Insuline	Autoimmune Obesity
Central DI	Polydipsia Polyuria ⊕ Nocturnal Sx	Hypotonic Urine	Corrects with ADH	Desmopressin	Trauma, Stroke, Tumor Granulomas
Nephro DI	Polydipsia Polyuria ⊕ Nocturnal Sx	Hypotonic Urine	Does Ø Correct	Diuretics	Lithium Demeclocycline
Psychogenic Polydipsia	Polydipsia Polyuria Ø Nocturnal Sx	Hypotonic Urine	Corrects with Water Restriction	Stop drinking so much water	Psychiatric Disease

THYROID NODULES

Thyroid Nodules

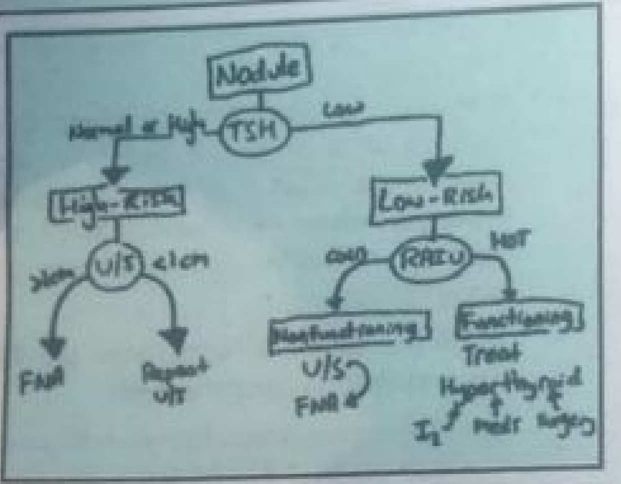
- Thyroid nodules are prevalent; up to 60% of patients have them and they increase with age. Your job will be to determine **"is this a cancer or not?"**
- **The physical exam** can be revealing: a **fixed, hard nodule** with **non-tender lymph nodes** is suspicious for malignancy, while a soft, mobile nodule with pain is suggestive of something else.
- Risk factors are listed to the right.
- The diagnosis is best made with labs and imaging. There are several tools at our disposal.
- The **Fine Needle Aspiration** (FNA) is the **best test** to assess a thyroid nodule; it's a biopsy. However, it should be near the end of the diagnostic tree.
- The risk of a functioning nodule (that is, any nodule that secretes T4) being cancer is quite low.
- So the **first test** that should be obtained after a nodule is discovered is a **TSH**.
- If the **TSH is low** (which means the nodule is secreting T4), it should be followed with a **RAIU** scan.
- If indeed the nodule lights up **"hot,"** this confirms suspicion of a hyperfunctioning nodule. It can be treated **as hyperthyroidism** – medications to suppress, radioactive iodine ablation or surgery to cure.
- But if the nodule is **"cold,"** then the **T4** was coming from somewhere else.
- Here, the nodule is NOT hyperfunctioning; it needs to be biopsied with an FNA. Whenever a biopsy is being considered, an **ultrasound should be done first**.
- The **risk of malignancy** is much higher if the **TSH was high or normal** on that **original TSH test.**
- A RAIU isn't indicated as it's unlikely to reveal a hot nodule.
- Instead, the next step is **ultrasound**. If the lesion is **small** ***(< 1cm for solid, < 2cm for cystic)*** and has non-malignant features, it can be followed with repeat ultrasound months later.
- If the lesion is **large** or has malignant features, it should be biopsied with the FNA.

Pre Test Risk of Malignancy

History	Physical
Radiation to head and neck	Fixed, hard, firm
Personal History of Thyroid Cancer	Nontender Lymph Nodes
Hoarseness	Painless
Age < 20	
Age > 60	

Tests for Thyroid Nodules

Test	Use
TSH	First test always
RAIU	If TSH depressed
U/S	Prior to FNA
FNA	Best Test



FNA results

FNA Results	Action
Malignancy	Prompt Surgery
Benign	Repeat U/S 6 - 12 months
Inconclusive	Repeat FNA immediately

- Risk of malignancy is dependent both on the **size** and the **risk** of the nodule and patient.
- FNA is indicated if a **solid hypoechoic nodule** is **> 1cm**.
- FNA can be deferred if the nodule is lower risk; **as an example a 2cm** may be the cut-off for a cystic lesion.
- FNA can be prescribed for a smaller lesion if the patient is high risk; as an **example a 5mm nodule** in someone with radiation to the head and neck.
- If the FNA shows a **malignancy** the thyroid must be removed (**surgery**).
- Deciding between hemi and total thyroidectomy is beyond the scope of this course.
- If the FNA reveals **benign tissue**, then the nodule should be followed with **ultrasound** and rebiopsied if it changes in size.
- If the FNA is **inconclusive**, the FNA should be repeated.

Cancers	Need-to-know
Papillary	Most common thyroid cancer, associated with XRT Orphan-Annie Nuclei and Psammoma Bodies Papillary Architecture (FNA), h/o Head and Neck Ca Positive Prognosis (Slow Growing) → **Resection**
Follicular	Tumor difficult to diagnose on biopsy, looks normal Spreads hematogenously, tx **resection & I2 ablation**
Medullary	C-Cells producing Calcitonin = Hypo-Ca Part of MEN2a and MEN2b genetics
Anaplastic	Found in elderly patients Grows locally and quickly Dismal Prognosis correlated with degree of Anaplasia

THYROID DZ + APPROACH

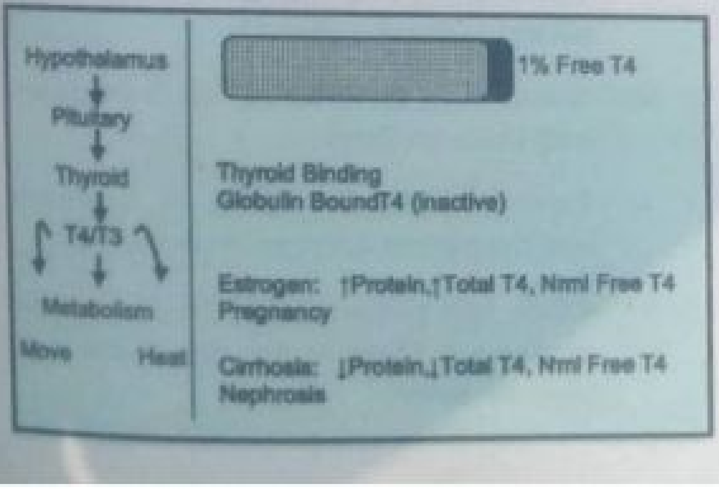
Physiology

- **TRH** is secreted by the hypothalamus.
- It stimulates the anterior pituitary to make **TSH.**
- TSH stimulates the thyroid to make **T4**/T3 in a 10:1 ratio.
- T3 is **more potent** than T4; T4 is converted into T3 in the periphery to exert its effects.

- Most of the T4 is **inactive**, bound to **Thyroglobulin Binding Protein**.
- Only 0.1% is free and active.
- **Free T4** is tightly regulated and **doesn't** change in the absence of thyroid disease.
- **Total T4** changes with alterations in **protein** (pregnancy, OCPs, cirrhosis, nephrosis).
- The effect of T4/T3 is to ↑ metabolism (**catabolic** and **thermogenic**).

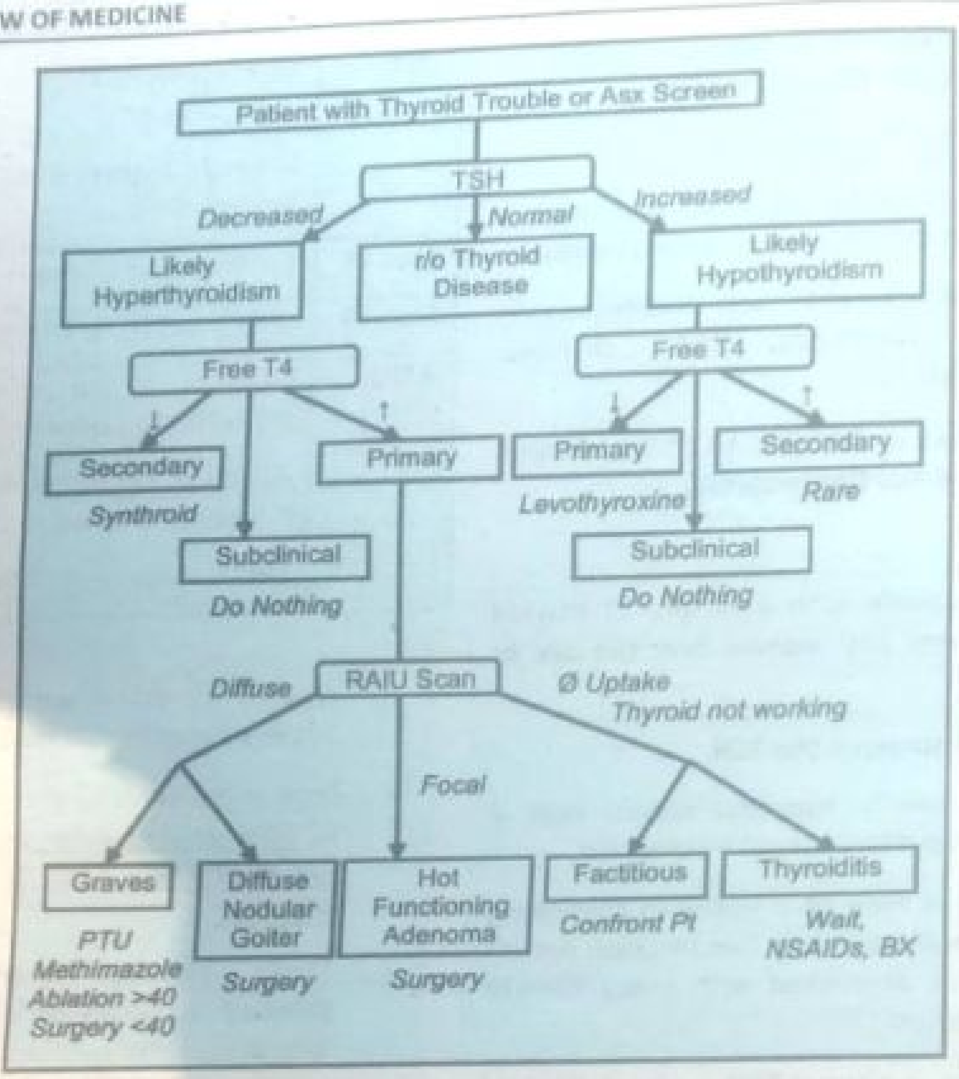
Tests

- **Screen** people with a history of thyroid disease and any **woman over the age of 50**.
- The best screen is the **TSH**.
- If it's: low = hyperthyroidism, high = hypothyroidism, normal = euthyroid.
- Looking at **Free T4** is useful in confirming an atypical screening TSH because there's a disease associated with every TSH+T4 combination.
- However, a **normal TSH means Euthyroid** (highly sensitive).
- **Do NOT** get a Free T4 if TSH is normal; instead, ignore the Free T4 if TSH is normal.
- Sick people can get what's called **sick euthyroid syndrome** (they're sick, T4 is wacky but TSH is normal), but there's no need do anything.


Hypothalamus
Pituitary
Thyroid
T4/T3
Metabolism
Move
Heat
1% Free T4
Thyroid Binding Globulin BoundT4 (inactive)
Estrogen: ↑Protein,↑Total T4, Nml Free T4
Pregnancy
Cirrhosis: ↓Protein,↓Total T4, Nml Free T4
Nephrosis

TSH	Best Screening Test. ↑ Hypothyroid, ↓ Hyperthyroid Normal = Euthyroid. Some states can fool you, so...
Free T4	Confirms TSH findings
Free T3	Only if ↓ TSH and normal or ↓ T4
RAIU	Evaluate a 1o Hyperthyroidism. Differentiates between causes of hyperthyroid. May not be necessary with a good story

- **Free T3** is pretty much useless unless you suspect hyperthyroid despite a normal T4.
- Look at the chart to the right. What it says is, ***"the only diseases that really matter are High TSH + Low T4 and Low TSH + High T4."***
- That's **primary hypothyroidism** and **primary hyperthyroidism**. If there's a primary hypothyroidism, simply give synthroid.
- When a **hyperthyroid** patient is encountered a **RAIU scan** can help with a diagnosis.
- Radiolabeled Iodine is picked up by ***active thyroid tissue*** which lights up = "**hot**" while ***inactive tissue*** does not = "**cold.**"
- Finally, there are **antibodies** that when present in some diseases are **specific** (but they're **not sensitive**). While helpful, they're academic rather than confirmatory.
- Confirmation is made by **FNA Biopsy**.
- More on Biopsying and RAIUs in the thyroid nodule section.


Patient with Thyroid Trouble or Asx Screen
TSH
Decreased
Normal
Increased
Likely Hyperthyroidism
r/o Thyroid Disease
Likely Hypothyroidism
Free T4
↓
↑
Secondary
Synthroid
Subclinical
Do Nothing
Primary
Free T4
↓
↑
Primary
Levothyroxine
Secondary
Rare
Subclinical
Do Nothing
RAIU Scan
Diffuse
Ø Uptake
Thyroid not working
Focal
Graves
PTU
Methimazole
Ablation >40
Surgery <40
Diffuse Nodular Goiter
Surgery
Hot Functioning Adenoma
Surgery
Factitious
Confront Pt
Thyroiditis
Wait, NSAIDs, BX

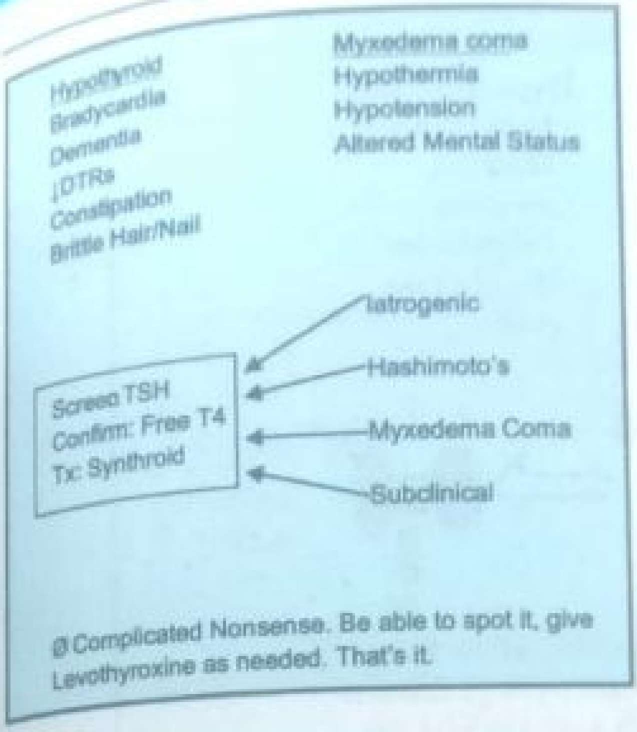
HYPOTHYROIDISM

Introduction

- **Hypothyroidism** is a product of ↓metabolism secondary to ↓T4.
- This causes the patient to slow down.
- A variety of things slow: heart (**bradycardia**), mind (**dementia**), reflexes (↓ **DTRs**), bowel function (**constipation**), and metabolism (**weight gain**).
- Hypothyroidism is easier than hyperthyroidism because regardless of how they got there, there's only one treatment - **Levothyroxine**.
- Screen with **TSH** (it'll be elevated). Confirm with **T4** (it'll be low) and replace as needed.
- Don't do any **biopsies** or **RAIU scans** as they are extraneous.

Iatrogenic

- The **most common** cause of hypothyroidism is **iatrogenic**.
- We treat hyperthyroidism and cancer with ablation or surgery, leaving the patient without a thyroid.
- This is why close follow up is necessary with these patients.
- Eventually, the circulating T4 diminishes and the patient becomes hypothyroid.
- When the patient's TSH begins to rise, exogenous **T4** must be substituted with **Levothyroxine**.


Hypothyroid
Bradycardia
Dementia
↓DTRs
Constipation
Brittle Hair/Nail
Myxedema coma
Hypothermia
Hypotension
Altered Mental Status
Iatrogenic
Hashimoto's
Myxedema Coma
Subclinical
Screen TSH
Confirm: Free T4
Tx: Synthroid

Ø Complicated Nonsense. Be able to spot it, give Levothyroxine as needed. That's it.

Hashimoto's

- The **most common disease** that causes hypothyroidism is Hashimoto's.
- It's caused by a **lymphocytic infiltrate** secondary to antibodies (**Antithyroid Peroxidase** and **antithyroglobulin 90% Specific**).
- The only way to definitively diagnose is with a biopsy, but because Hashimoto's is **irreversible** and the patient presents with hypothyroidism, just treat the hypothyroid.
- The natural course of the disease is a period of transient hyperthyroidism followed by transient hypothyroidism.

Myxedema Coma

- If the **hypothyroid** gets **really bad,** or there's a precipitating event, everything shuts down.
- Like thyroid storm this is a **medical emergency.** This time it's characterized by **hypothermia, hypotension,** and **coma.** Initiate supportive care (**IVF, Warming Blankets**) and give **high-dose T4.** Because peripheral conversion is impaired, also give straight up **T3** if **T4 fails** or symptoms are severe from the start.

Subclinical

- If the **↑ TSH + Normal T4/T3,** the patient needs to be followed.
- If **Ab positive** they'll eventually progress to hypothyroid.
- If **Ab negative** they might get better.
- There's no consensus on when to start treatment, but generally make the patient happy by **treating when symptoms start** and treat everyone with **overt hypothyroidism** (TSH>10).

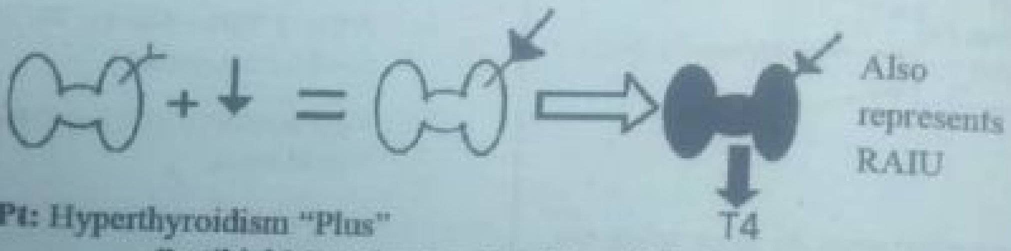
HYPERTHYROIDISM

Introduction

- Hyperthyroidism is caused by too much T4.
- It can come either from **overproduction** as in Graves, **exogenous intake** (factitious or struma ovarii), or **↑release** as in Thyroiditis.
- The symptoms are **↑ metabolism** (heat intolerance, diarrhea, sweating, palpitations, tachycardia, Afib, and Weight Loss).
- Determining a definitive diagnosis may require a **biopsy,** but it's usually not necessary.

Thyroid Storm
- Fever
- Delirium
- Hypotension

Hyperthyroidism
- Heat Intolerance
- Diarrhea
- Sweating
- Palpitations
- Weight Loss
- Afib



Pt: Hyperthyroidism "Plus"
- Pretibial Myxedema = Swelling of the Feet
- Ophthalmopathy = Proptosis + Exophthalmos

Dx: ↓ TSH, ↑ T4, Diffuse RAIU ↑, ⊕ Anti-Thyroid Ab

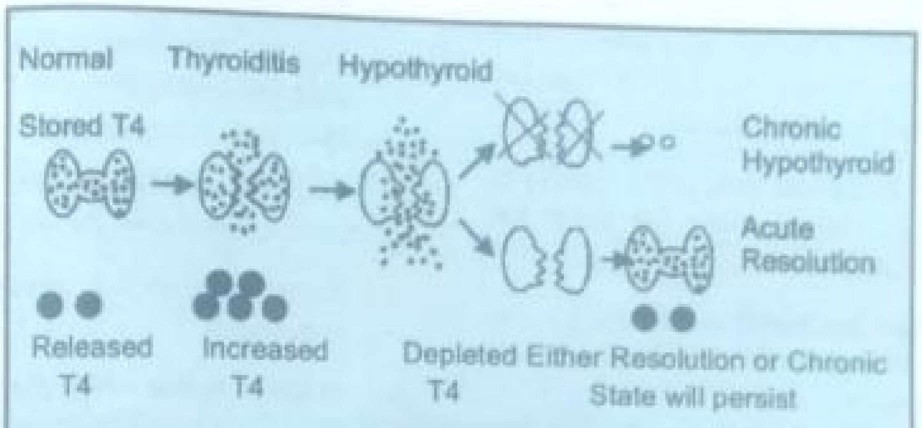
Tx: Acute: Propranolol to control adrenergic symptoms
PTU or Methimazole to quell hyperthyroid state
Chronic: Radioablation with radioactive iodine
Surgery if Pregnant

F/u: Synthroid when hypothyroid, after treatment
Steroids/Radiation for Ophthalmopathy, if worsens

11 Graves

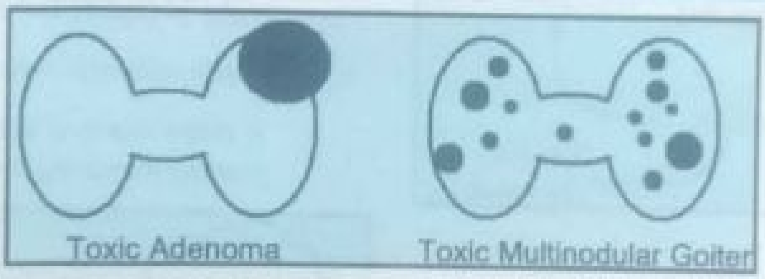
- An **autoimmune disease** caused by **thyroid stimulating antibodies** that mimic TSH and cause proliferation of cells as well as ↑ production of T4.
- This causes a **diffuse homogeneous** enlargement of the thyroid. It's the **most common cause** of hyperthyroidism.
- Beyond the usual hyperthyroid condition there can also be **pretibial myxedema** and **ophthalmopathy (proptosis and exophthalmos)** - both unique to Graves.
- It's essentially a clinical diagnosis, but **thyroid labs will show: ↓ TSH, ↑ T4**, and a **Diffuse RAIU**.
- **Antibodies** (80% Sp, Ø Se) can be checked; but the focus should be on treatment.
- Control their **symptoms** with **propranolol**.
- To help them out of a hyperthyroid state use **PTU** (safe in **pregnancy**) or **Methimazole**.
- Be careful not to start these drugs if awaiting RAIU or ablation.
- These patients require definitive therapy: **Radioactive Iodine Ablation** or **Surgery** (usually if pregnant, 2nd trimester surgery).
- Since this will make them **hypothyroid** follow up and start **synthroid** when hypothyroid.

- Finally, the **ophthalmopathy** may worsen despite treatment; treat it with **steroids** or radiation.


Normal
Thyroiditis
Hypothyroid
Stored T4
Chronic Hypothyroid
Acute Resolution
Released T4
Increased T4
Depleted T4
Either Resolution or Chronic State will persist

Thyroiditis

Acute: trauma, infection, drugs	Supportive	Resolution
Subacute: Silent = Lymphocytic ⊕ TPO	Antibodies	Resolution
Painful = Viral Granulomas	Supportive	
Chronic: Hashimoto's	NSAIDs Steroids	Resolution Hypothyroid


Toxic Adenoma
Toxic Multinodular Goiter

2) Thyroiditis

- In an inflammatory process, even **destructive ones**, the **first step** is to break open the cells and **release stored T4**.
- This causes a **transient hyperthyroidism**.
- If the insult is **acute (infection/trauma) or subacute (subacute thyroiditis)** the thyroid will recover - sometimes with a period of hypothyroidism. Rarely does this require intervention.
- If **chronic (Hashimoto's),** destruction wins = persistent hypothyroidism. Because TSH/T4 looks like Graves, differentiate with **RAIU** (cold inactive thyroid) and **ESR/CRP** (elevated in Hashimoto's only).

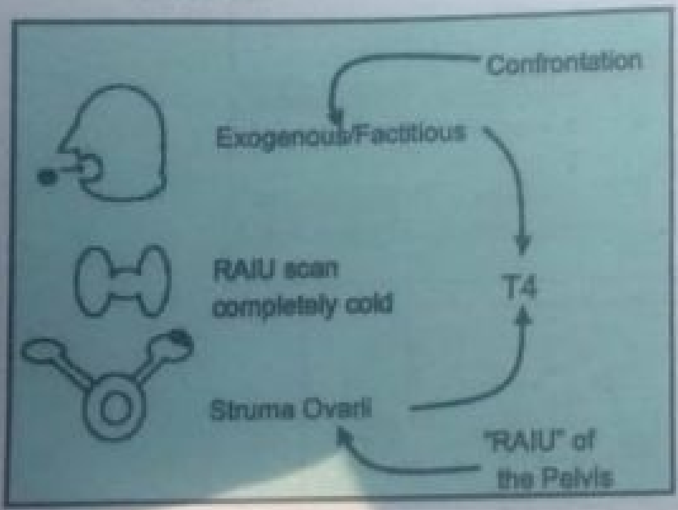
3] Toxic Multinodular Goiter or Adenoma

- For whatever reason, **autonomous nodules** referred to as "**hot**" produce T4 without an off switch.
- Rarely cancer (see workup for thyroid nodules), nodules can usually be seen on **RAIU** or felt on an **exam**. Because the rest of the thyroid senses too much T4 it shuts off, so only the toxic nodules light up.
- *"Toxic" means "Makes T4."*

4] Factitious and 5] Struma Ovarii

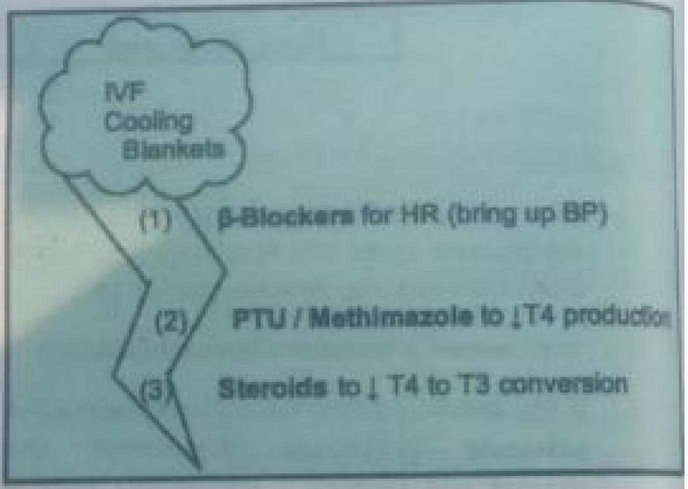
- If someone that's normal to begin with gets levothyroxine the thyroid will **shut off** (**↓ TSH Ø RAIU**). Still, the T4 will remain high. The only way this can happen is if she's taking it **exogenously** (as in **Synthroid** to lose weight or we dosed a hypothyroid patient with too much of it) or if there's a **tumor somewhere** other than the thyroid (usually a dermoid cyst/teratoma of the ovary).

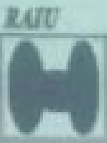
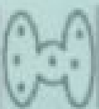
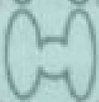
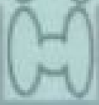
- Use the **Sestamibi scan** of the ovaries to r/o tumor then confront her about her factitious disorder.
- These two are together because 1 - the RAIU is normal and 2 - on the test both will be woman.

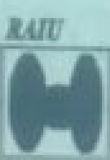
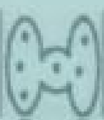
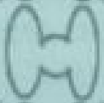
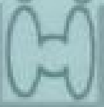

Confrontation
Exogenous/Factitious
RAIU scan completely cold
T4
Struma Ovarii
"RAIU" of the Pelvis

6) Thyroid Storm

- When the hyperthyroidism gets out of control it's a life threatening **emergency**.
- It's a clinical diagnosis - defined by someone with hyperthyroidism plus **alarm symptoms = fever, delirium,** and **hypotension.**
- They have such heat intolerance that they burn up and such tachycardia that there's hypotension.
- After making the diagnosis start immediate supportive therapy with IVF and **cooling blankets.**
- To treat, start **Propranolol** (β-Blockers) to slow the heart down and get the BP back up.
- Give **PTU or Methimazole** to reduce the production of new thyroid hormone.
- Finally, **steroids** will reduce the T4 to T3 conversion.
- In storm, **Iodide** can be given.
- The thyroid can **either** pick up Iodide or make Thyroid Hormone; it preferentially picks up Iodide.
- For a temporizing measure, use Iodide to ↓ T4.
- If not fixed that Iodide will be used to make T4 (**Iodide Escape**).
- That'll make the patient worse.
- A single storm is indication for definitive therapy (removing the thyroid altogether).


IVF
Cooling
Blankets
(1) β-Blockers for HR (bring up BP)
(2) PTU / Methimazole to ↓T4 production
(3) Steroids to ↓ T4 to T3 conversion

Disease	*Path*	*Patient*	*TSH*	*T4*	*RAIU*	*Diagnosis*	*Treatment*
Graves	Autoimmune stimulating antibodies	Hyperthyroid +ophthalmopathy +Pretibial Myxedema	↓	↑		Anti-TSH-R Antibody	Propranolol PTU/Methimazole Radioactive Ablation Surgery
Thyroiditis Painless Subacute Lymphocytic +TPO Painful Subacute Granuloma Viral Chronic Lymphocytic		Either painful or painless transient hyperthyroidism that may persist	↓	↑	N/A	Bx for Infiltrate Anti-Peroxidase Antibody (TPO)	NSAIDs Wait Synthroid if Hypothyroid
Toxic Goiter	Autonomous Nodules Secrete T4	Hyperthyroid with palpable nodules	↓	↑		Bx if suspicious for cancer	
Factitious	Exogenous T4, Oral	Hyperthyroid, often in a woman	↓	↑		Confrontation	Stop taking exogenous T4
Struma Ovarii	Ovarian tissue Dermoid Cyst produces T4	Hyperthyroid, always in a woman	↓	↑		"RAIU" of the Ovaries, Sestamibi Scan	Remove the Cyst
Thyroid Storm	Super mega ultra hypothyroidism	Hyperthyroid ⊕ CHF ⊕ AMS ⊕ Fever	↓↓	↑↑	Any, no one diagnostic	Diagnosis Ø Needed Just Treat, and treat fast	IVF, Cooling Blankets, Steroids, Propranolol, PTU, Iodide

Disease	*Path*	*Patient*	*TSH*	*T4*	*RAIU*	*Diagnosis*	*Treatment*
Graves	Autoimmune stimulating antibodies	Hyperthyroid +ophthalmopathy +Pretibial Myxedema	↓	↑		Anti-TSH-R Antibody	Propanolol PTU/Methimazole Radioactive Ablation Surgery
Thyroiditis Painless Subacute Lymphocytic +TPO Painful Subacute Granuloma Viral Chronic Lymphocytic		Either painful or painless transient hyperthyroidism that may persist	↓	↑	N/A	Bx for Infiltrate Anti-Peroxidase Antibody (TPO)	NSAIDs Wait Synthroid if Hypothyroid
Toxic Goiter	Autonomous Nodules Secrete T4	Hyperthyroid with palpable nodules	↓	↑		Bx if suspicious for cancer	
Factitious	Exogenous T4, Oral	Hyperthyroid, often in a woman	↓	↑		Confrontation	Stop taking exogenous T4
Struma Ovarii	Ovarian tissue Dermoid Cyst produces T4	Hyperthyroid, always in a woman	↓	↑		"RAIU" of the Ovaries, Sestamibi Scan	Remove the Cyst
Thyroid Storm	Super mega ultra hypothyroidism	Hyperthyroid ⊕ CHF ⊕ AMS ⊕ Fever	↓↓	↑↑	Any, no one diagnostic	Diagnosis Ø Needed Just Treat, and treat fast	IVF, Cooling Blankets, Steroids, Propranolol, PTU, Iodide

EPIDEMIOLOGY

SCREENING

- Screening is generally looking for cancer and medical disease.

Cancers we screen for

- Currently, there are only **four cancers** for which screening is recommended. Grade for practice is included in parentheses.

Grading Scale
A = Definitely do this
B = Probably do this
C = Probably don't do this
D = Don't do this
I = Insufficient evidence

- For **colon cancer**, a **colonoscopy** is the preferred screening tool. **Fecal immunochemical test (FIT)** is more specific than guaiacbased testing as it only detects globins that are present (not seen in foods and already digested in upper GI bleeds, but they're effectively the same, FIT = FOBT for you.
- In 2016, **breast cancer** screening recommendations were changed. Testing at 40 years is still an option (Grade C) after discussion with patient (taking into account false positives, stress/anxiety of screen, family hx). The benefit of screening seems to be higher for those in their **50s and 60s**.
- **Lung cancer** screening with a **low dose CT scan** is a fairly new recommendation; it only applies to individuals with a **30 pack year** cigarette history within the last 15 years.
- **Cervical cancer** continues to **start screening at 21** even as that age group fills with women that have the HPV vaccine.

Can space out to every 5 years if combined with HPV testing at age 30.

Cancer	Age	Screen
Colon	50-75 yrs (A)	Colonoscopy q10 yrs OR Flex Sig q5 + FOBT q3 yrs OR Guaiac FOBT q1 yr
	> 75	If they're doing great otherwise
	>85	Stop no matter what
Breast	~~Start 40 (C)~~ Start 50 (B) Stop> 75yrs	~~Mammogram q1y~~ Mammogram q2y
Cervical	21-65 yrs (A) 65	Pap Smear q3 yrs OR HPV + Pap q5 yrs (over 30) If abnormal keep going
Lung	55-80 yrs + 30 py + Quit < 15 yrs (B)	Low dose CT q1y Or 15y from quit

Cancers we don't screen for

- We don't screen for other cancers because a) we don't have a screening tool that is cost effective or b) improves mortality. Most notable is **prostate cancer**. It was previously screened annually by PSA + digital rectal exam. However, the USPSTF changed its recommendation a few years back as there's minimal benefit given the potential harm. Most men die with prostate cancer – not from it. Another example is **ovarian cancer** in average risk patients. The only screen we have finds it too late – at stage 3 or worse – so there's no benefit.

Don't routinely screen for these cancers
- *Grade D = ovarian, prostate, testicular, pancreatic*
- *Grade I = skin, bladder, oral*

2015-2016 significant changes
- *Thyroid dysfunction screening now Grade I*
- *Visual acuity screening in 65+ yrs now Grade I*

Medical diseases we screen for

- In order to get these questions right on the test, you have to identify the person who needs the screen and how to do it.
- The most likely ones to show up are the one time screens: hepatitis C, osteoporosis, and AAA.

**These recommendations are based on the latest U.S. Preventive Services Task Force (USPSTF) guidelines as of 12/2016. Everyone has different reqs, but standardize with these. We strive to keep this document up to date but all recs can be found here.*

Dz	Age	Screen
AAA	♂ 65-75 yrs + smoke	One-time U/S of abdominal aorta
Osteoporosis	♀ 65 yrs (B) and ♂	DEXA scan (one-time if normal)
Hepatitis C	Adults born between 1945-65 (B)	One-time antibody screen
HIV	15-65 yrs (A)	One-time rapid test, if ↑ risk
Hypertension	Everybody (A)	Check BP (every time)
Diabetes	HTN (B)	A1c
Cholesterol	♀ 45 yrs (A) and ♂ 35 yrs (A) Start at 20 yrs for both if high risk (B)	Fasting lipid panel q5 yrs
Depression	Everybody (B)	PHQ, EPDS, etc.

VACCINATIONS

Introduction

- Vaccines are essential in preventing disease. Remember the basics but know that recommendations change annually due to breakthroughs and additional data. The **only absolute contraindication to immunizations is anaphylaxis** with previous administration. Others (like mild to moderate illness) should not prevent administration.

Note that these are the American requirements – if you leave the continent the list gets longer as you add on vaccines for tropical diseases.

Previous anaphylaxis with immunization? Don't give it again.

Test-Worthy Notes and Happenings

- The **HPV immunization** can be given as early as 9 years of age and is recommended for both boys and girls. In practice, giving the vaccine early scares parents – stress that it's to build the immune response well before being sexually active. **It doesn't increase promiscuity**.
- **Egg allergy** is **NOT a contraindication** to **influenza vaccine**. True anaphylaxis can receive the recombinant vaccine if 18 yrs. If reaction is non-anaphylactic, the inactivated vaccine may be given with 30 minutes of observation after administration. Also, MMR doesn't have significant cross-reactivity with any egg allergy - it may be given (see Peds – Vaccinations).

Trendy news: the CDC's Advisory Committee on Immunization Practices (ACIP) recommended that the live attenuated influenza vaccine (LAIV) not be used during the 2016-17 flu season due to concerns over its efficacy. Won't be tested but good clinical info.

Pneumococcal immunization is now infinitely confusing as there are now 23 and 13 valent doses which need to be considered. Per current schedule, 13 series is being completed in childhood. There must be a one-year gap between 13 and 23 administration with an exception: immunocompromised, asplenic, CSF leak, and cochlear implants may receive 23 at least 8 weeks after 13 administration. **"13 before 60, 23 after 65".**

Pneumococcal guidelines

-Don't give 23 and 13 at same visit (for most part, need 1 yr gap)

-13 series completed in childhood

-13 and 23 continued if high risk conditions

-Give 13 first if both are needed

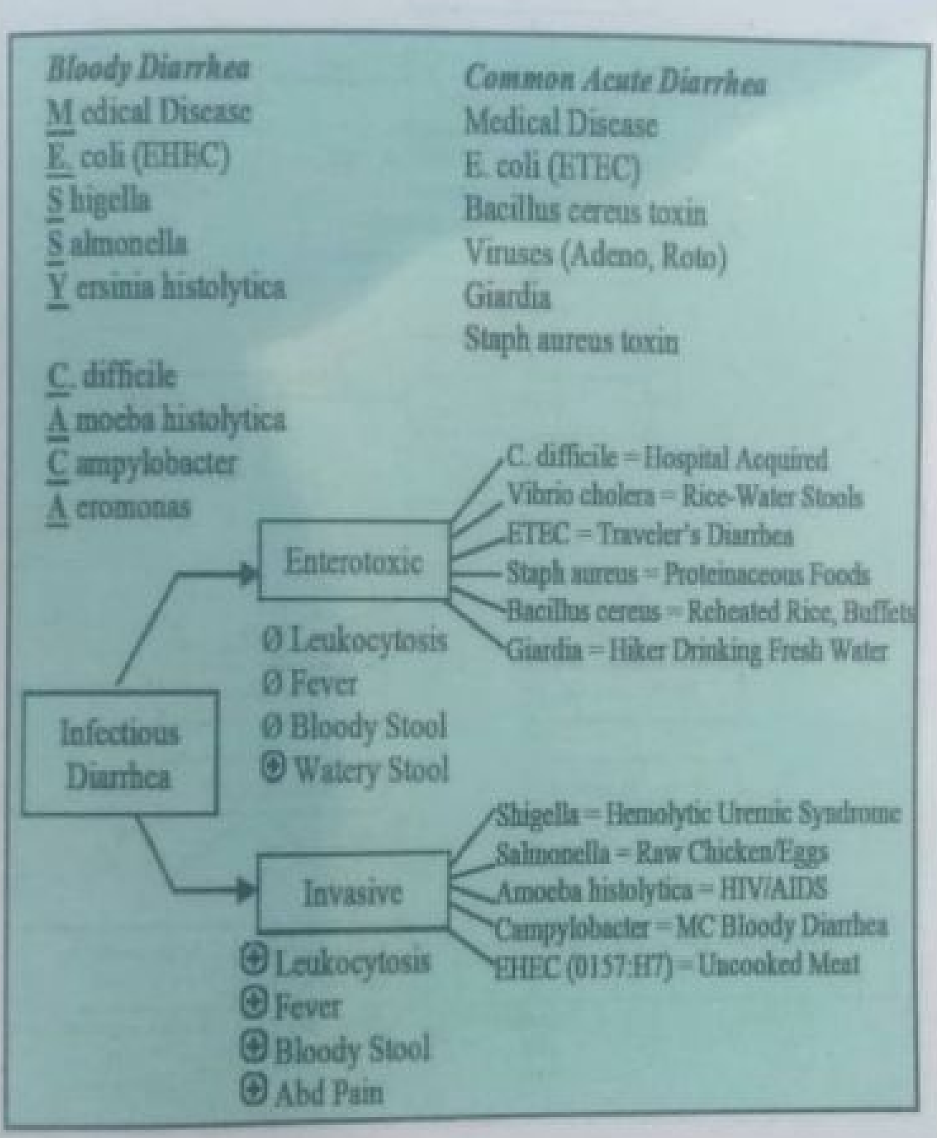
Vaccine	Age/Frequency	Appropriate	Contraindicated
Tdap	q 10 yrs	> 3 doses – Clean & > 10 yr - Tdp – Dirty & > 5 years - Tdap < 3 dose – Clean Wound - Tdap – Dirty Wound - Tdap+TIG	Encephalopathy c̄ previous administration
Pneumococcal	Complete 13 as a kid Get 23 for old people or kid with risk factors	"13 before 60, 23 after 65"	Do not give 23 and 13 at same visit
Zoster	Once p̄ 60	Everybody regardless of previous varicella dz	Severe immunodeficiency (Live Attenuated)
Hep A/B	Usually completed in childhood	Hep A x 2 Hep B x 3 Pick up where you left off	ø
Meningococcus	Age 11	College, military, Hajj to Mecca	ø
HPV	♀ and ♂ 9-26 yrs	Everyone. It prevents cancer	ø
MMRV	All Children	All Children	↓ immune system Pregnancy
Influenza	Annually	Everybody	If Anaphylactic rxn to egg Can use if only rash Else use recombinant if >18 yrs

GASTROENTEROLOGY

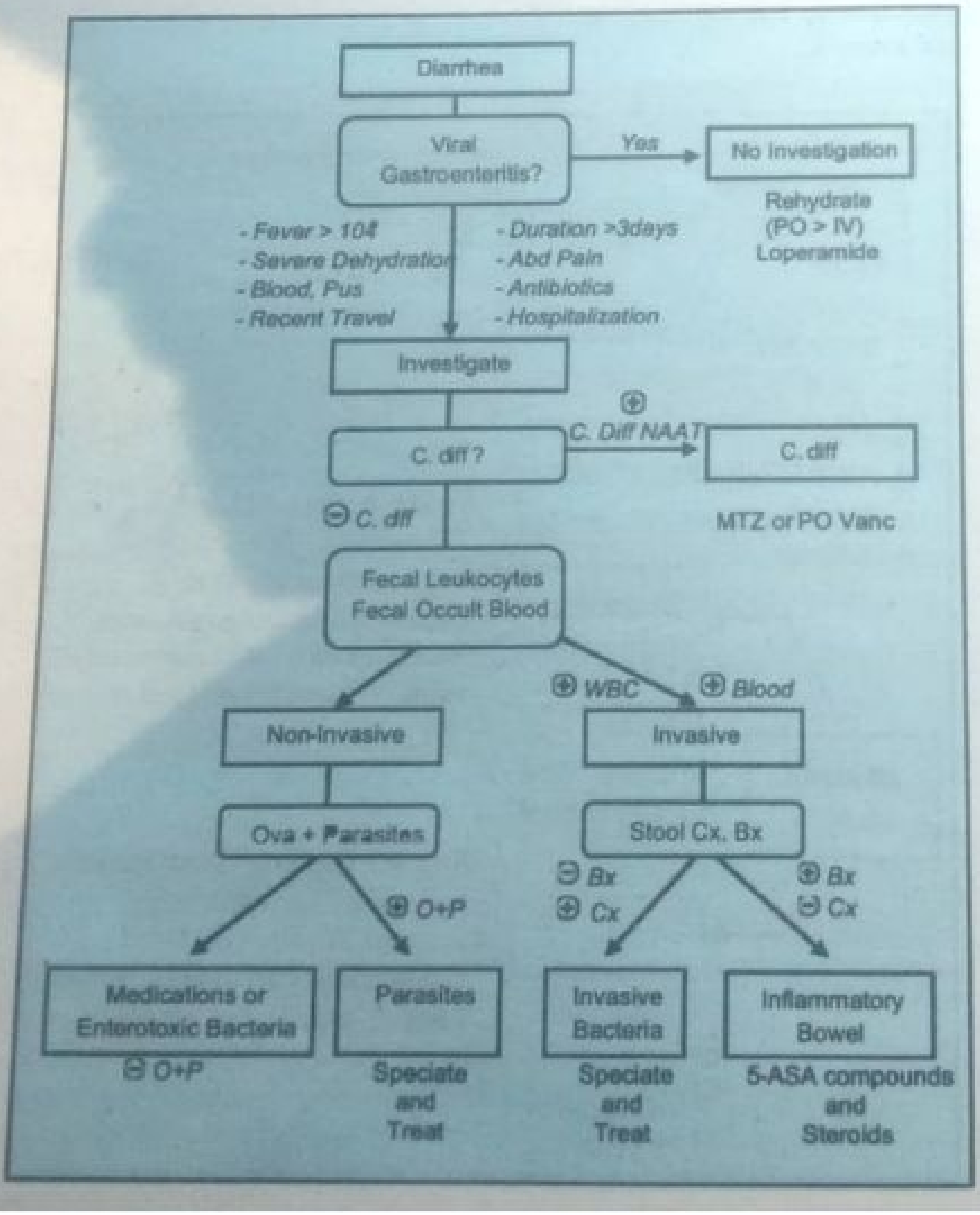
ACUTE DIARRHEA

Introduction and Definitions

- Diarrhea itself is defined by **> 200g stool / day**. Unfortunately, no one is going to measure their stool every day in a bucket at dry weight.
- Clinically, it's defined as ↑ **frequency** or ↓ **consistency** of stools.
- **Acute diarrhea** is any diarrhea with a duration **< 2 weeks.**
- **Chronic diarrhea** is a duration > 4 weeks.
- **Subacute** is "in between."
- When talking about an **acute diarrhea** it really means **infectious diarrhea.**
- Most causes of diarrhea are infectious and **self-limiting.** It's your job to know when to do additional tests and when to give antibiotics. In real life, that's rarely ever.


Bloody Diarrhea
M edical Disease
E. coli (EHEC)
S higella
S almonella
Y ersinia histolytica
C. difficile
A moeba histolytica
C ampylobacter
A eromonas
Common Acute Diarrhea
Medical Disease
E. coli (ETEC)
Bacillus cereus toxin
Viruses (Adeno, Roto)
Giardia
Staph aureus toxin
Infectious Diarrhea
Enterotoxic
Ø Leukocytosis
Ø Fever
Ø Bloody Stool
⊕ Watery Stool
C. difficile = Hospital Acquired
Vibrio cholera = Rice-Water Stools
ETEC = Traveler's Diarrhea
Staph aureus = Proteinaceous Foods
Bacillus cereus = Reheated Rice, Buffets
Giardia = Hiker Drinking Fresh Water
Invasive
⊕ Leukocytosis
⊕ Fever
⊕ Bloody Stool
⊕ Abd Pain
Shigella = Hemolytic Uremic Syndrome
Salmonella = Raw Chicken/Eggs
Amoeba histolytica = HIV/AIDS
Campylobacter = MC Bloody Diarrhea
EHEC (0157:H7) = Uncooked Meat

- **Invasive** bacteria get into the mucosa which causes **fever + leukocytosis**. They destroy the endothelium and produce a **bloody diarrhea** with **WBC in stool**. This is easy to spot but may be confused for one of the chronic diarrheas, as they can cause an inflammation as well. **Lactoferrin** is the most sensitive test.
- **Enterotoxic** bacteria produce a compound that turns the absorptive gut to a **secretory gut**. This may be in the form of an **active toxin** (vibrio) or a **preformed toxin** (staph). In any case, there's **no fever, leukocytosis, or blood** but there is **watery stool**. The history can alert and point to a specific agent; corresponding antigens should be investigated (reheated rice, protein dip, shellfish). However, because this person is pooping a lot right now, there's little ability to trace their last 72 hrs of eating, presuming there was a preformed toxin somewhere in their history (it's likely they will have risk factors for several organisms in any given 72 hr period). Since these are usually self-limiting, treatment centers around **hydration and loperamide**.
- **Be cautious -Do NOT give loperamide** to diarrhea resulting from an invasive organism as it will make it worse!


Diarrhea
Viral Gastroenteritis?
Yes
No Investigation
Rehydrate (PO > IV) Loperamide
- Fever > 104
- Severe Dehydration
- Blood, Pus
- Recent Travel
- Duration >3days
- Abd Pain
- Antibiotics
- Hospitalization
Investigate
⊕ C. Diff NAAT
C. diff?
C. diff
MTZ or PO Vanc
⊖ C. diff
Fecal Leukocytes Fecal Occult Blood
⊕ WBC
⊕ Blood
Non-Invasive
Invasive
Ova + Parasites
Stool Cx, Bx
⊕ O+P
⊖ Bx
⊕ Cx
⊕ Bx
⊖ Cx
Medications or Enterotoxic Bacteria
⊖ O+P
Parasites
Speciate and Treat
Invasive Bacteria
Speciate and Treat
Inflammatory Bowel
5-ASA compounds and Steroids

C. Difficile

- C. diff is part of the normal gut flora. When exposed to **antibiotics**, C diff wins and causes diarrhea. It's diagnosed with a C. diff **NAAT** (**not** toxin, **not** colonoscopy).
- There are **two presentations**. The first is a **watery diarrhea** with a **tell-tale smell**. This is treated with oral medications. **Oral metronidazole** is essentially equivocal to oral **vancomycin**, but metronidazole is cheaper.
- For *repeated recurrences* use **fidaxomicin**.
- For *refractory cases* a **fecal transplant** can be performed.
- The *second presentation is severe* C. diff, presenting with toxic megacolon, **renal failure**, and **overt sepsis / shock**.
- This person requires **IV metronidazole AND oral vancomycin**.

Hemolytic Uremic Syndrome

- In the presence of **anemia** + **worsening Cr** + **Bloody Diarrhea** don't assume the Cr is rising from dehydration.
- Suspicion of Shigella and the Shiga toxin must be high. If suspected, get a **serum shiga toxin** assay and **E.coli O157:H7 culture.**
- Treatment is with supportive care, dialysis, and **plasma exchange**.

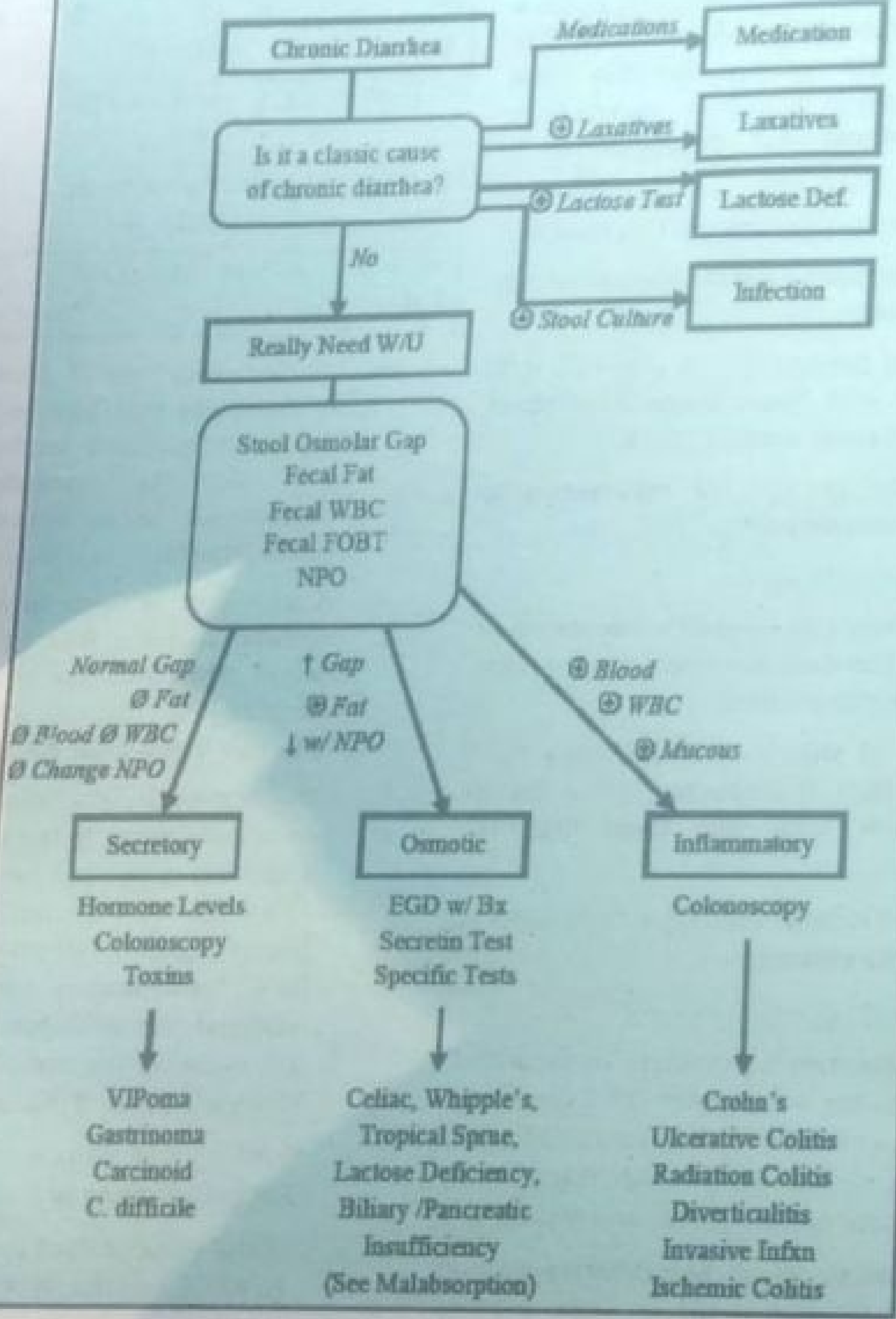
Secretory vs Osmotic vs Inflammatory

- Chronic diarrhea is persistent or recurrent symptoms for **> 4 weeks**; it's usually the result of a chronic underlying condition. It becomes initially important to differentiate pathologically and clinically.
- The **Osmotic Gap**, **Blood/Mucous**, and **Pattern of Bowel Habits** provide clues to clinically separate the different types.

Secretory	*Osmotic*	*Inflammatory*
Secretagogues: VIP, Gastrin, Toxins	Ø Absorption = Fat, Protein, Osmolar Load,	
Nrml Osmotic Gap	**↑ Osmotic Gap**	⊕ Blood
Ø Blood Ø Mucous	Ø Blood Ø Mucous	⊕ Mucous
⊕ Nocturnal Sxs	Ø Nocturnal Sxs	
Ø Change with NPO	⊕ Change with NPO	
Normal Fecal Fat	↑ Fecal Fat	

- The **Secretory** type of diarrhea is caused by molecules that transform the normal absorptive gut to a secretory one. This may be via **hormones** (VIPoma, Gastrinoma) or a persistent infection (**enterotoxins**).
- It produces an enterotoxigenic picture: **Normal Osmotic Gap** (not osmotic), no **blood** or **mucous** (not inflammatory), and because the toxin is already there, **no changes in BM after NPO**.
- The **Osmotic** diarrhea is caused by something being in the lumen that draws water out of the body and into the lumen. This is usually a product of **malabsorption** (lactose, gluten, fat, protein). There won't be an inflammatory picture (**no blood** or **mucous**), but something other than Na + K will make up the osmolarity of stool, thus there will be an **↑ Osmotic Gap**.
- Furthermore, tests will likely find **↑ Fecal Fat** (a byproduct of malabsorption).
- If the osmotic load is taken away (that is, go NPO), this diarrhea gets a lot better.

Measure Stool Osmoles (reported value)	Calculated Stool Osmoles (Stool Na + Stool K) *2	= Osmotic Gap
280	110	= 170, Osmotic
280	278	= 2, Secretory


Chronic Diarrhea
Medications
Medication
Is it a classic cause of chronic diarrhea?
⊕ Laxatives
Laxatives
⊕ Lactose Test
Lactose Def.
⊕ Stool Culture
Infection
No
Really Need W/U
Stool Osmolar Gap
Fecal Fat
Fecal WBC
Fecal FOBT
NPO
Normal Gap
Ø Fat
Ø Blood Ø WBC
Ø Change NPO
↑ Gap
⊕ Fat
↓ w/ NPO
⊕ Blood
⊕ WBC
⊕ Mucous
Secretory
Osmotic
Inflammatory
Hormone Levels
Colonoscopy
Toxins
EGD w/ Bx
Secretin Test
Specific Tests
Colonoscopy
VIPoma
Gastrinoma
Carcinoid
C. difficile
Celiac, Whipple's,
Tropical Sprue,
Lactose Deficiency,
Biliary /Pancreatic
Insufficiency
(See Malabsorption)
Crohn's
Ulcerative Colitis
Radiation Colitis
Diverticulitis
Invasive Infxn
Ischemic Colitis

- The **Inflammatory** diarrhea looks like acute inflammatory diarrhea: **+ Blood** and **+ Mucous.** But because it recurs, or has been chronic, it's likely due to a medical disease (like IBD).

Specific Diseases within Chronic Diarrhea

- **Osmotic** diarrheas deals with malabsorption syndromes.
- **Inflammatory** diarrhea is discussed in the acute diarrhea (Bloody Diarrhea) and in

the Inflammatory Bowel Disease content (Crohn's and UC).

- Some **secretory** diseases are here.

I. Gastrinoma

- Persistent **ulcers** despite treatment with **diarrhea** raise suspicion for **Zollinger-Ellison** syndrome and the presence of a **gastrin producing tumor.**
- First, measure a **serum gastrin** then allow for an **increased gastrin** on secretin stimulation.
- Do a **CT** scan or a **SRS** (Somatostatin Receptor Scintillography) to find the tumor, then **resect** (GI Gastric Disorders).

II. VIPoma

- Chronic diarrhea without a real presentation to go along with it.
- **High Serum VIP** is sufficient for diagnosis.
- **Resect it.**

III. Carcinoid

- A tumor usually found in the **small intestine** that has no symptoms until it **metastasizes to the liver.**
- Serotonin enters the blood stream causing **right heart failure, flushing,** and **Diarrhea.**
- Get a **Urinary 5-HIAA to confirm the** diagnosis and resect (GI Cancers).

CIRRHOSIS COMPLICATIONS

Definition and Introduction

- A cirrhotic liver is one that's been annihilated, replaced by **extensive fibrosis,** and now has minimal **regenerating nodules.**
- It's the **end-stage of liver disease** - regardless of the etiology.
- It produces a number of complications that become targets of therapy.
- Once cirrhotic, the only option is **transplant.**
- Knowing etiology, presentation, and the unique considerations is key to mastering cirrhosis.

Presentations and Labs

- The liver does a lot of things.
- It clears **bilirubin** - failure causes **jaundice** and **sclera icterus.**
- It produces **bile** - accumulation of bile causes **pruritus.**
- It also produces **coagulation factors** – a deficiency produces **bleeding.** Because all blood flow from the visceral organs flows through the liver, a cirrhotic liver, like a plug, ↑ resistance, which causes **portal hypertension.**
- This HTN causes **porto-caval shunting** (hemorrhoids, caput medusa, esophageal varices) and transudation of fluid (ankle edema and **ascites**).
- Ascites is exacerbated by a ↓ protein production (**hypoalbuminemia, Total protein ↓**).
- Estrogen is degraded and converted to testosterone while **estrogen excess** produces **gynecomastia,** palmar erythema, and spider angioma.
- Finally, the liver controls **ammonium** metabolism.
- Excess ammonium can cause **asterixis** (flapping tremor) and **encephalopathy.**
- Get an **Ultrasound** (1st , to identify cirrhosis), a **CT /MRI** to evaluate nodules or masses, and finally a **biopsy** (best) to confirm the diagnosis and etiology.
- **Acute hepatitis** causes an elevation of liver enzymes.
- A cirrhotic liver is burned out; the AST/ALT will be low or smoldering just above elevated.
- The **MELD score** (calculated using the bilirubin, INR, and creatinine) show how sick a liver is. 1 is normal, 40 is death. Transplant workup starts at 15.

- The full workup of a liver involves the LFTs (AST, ALT, Alk Phos, Bili, TP, Albumin), Coagulation Factors, Ultrasound, CT scan, and Transjugular Biopsy.

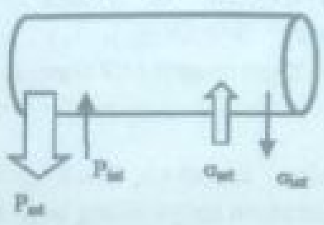
Ascites and SAAG

- Fluid in the abdomen (**ascites**) has multiple etiologies - one of which is cirrhosis.
- The patient will have **flank dullness**, a **fluid wave**, and **shifting dullness** on physical exam.
- To detect fluid an **Ultrasound** may be performed.
- Fluid may also be detected via **CT/MRI** (which helps with differentiation).
- What we worry about is a **1st time presentation** (etiology unknown) or a return customer with a fever or abdominal pain. For both cases do **paracentesis** first to get a **SAAG** score (Serum Albumin – Ascites Albumin) and an **AFTP** (cirrhosis vs cardiac ascites).
- If a SAAG is > 1.1 it's from portal HTN (**cirrhosis, R Heart Failure, Budd-Chiari**).
- If a SAAG is < **1.1** it's non-portal HTN related, with ↑ risk of TB and malignancy. The result will direct the workup. The goal is to treat the underlying causes.
- If secondary to cirrhosis, treat is by restricting fluid + salt and supplementing with diuretics.
- Everyone with ascites gets ↓ **Na Intake** (2g max/day), **limiting H_2O** (2L /day).

Cirrhosis Etiologies = "VW HAPPENS"	
Viral	Hep B/C
Wilsons	Eyes, Liver, Basal Ganglia (Cu)
Hemochromatosis	"Brooze Diabetes" (Fe)
Alpha-1 Anti-trypsin Deficiency	Emhysema and Cirrhosis
Primary Sclerosing Cholangitis	Men with Crohn's
Primary Biliary Cirrhosis	Women, Autoimmune, AMA, "Biliary Cirrhosis is for Bitches"
Ethanol	Drinkers
NASH/NAFLD	Fat people
Something Rare	

Also: Parotid Enlargement, Dupuytren's Contracture, clubbing, axillary hair loss

$$J = K(P_{art} - P_{int}) + (\sigma_{int} - \sigma_{art})$$



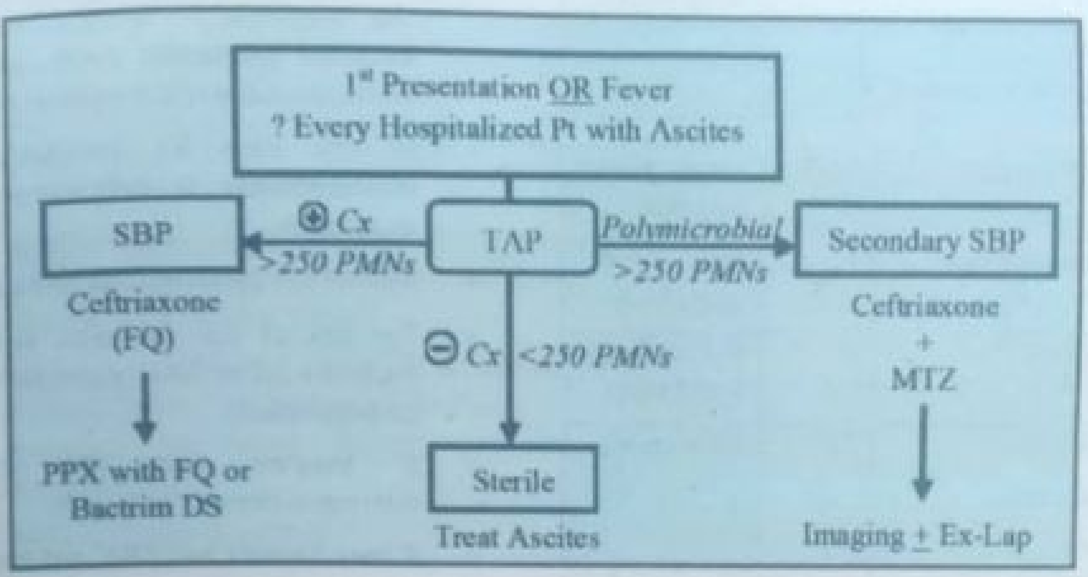
↑$P_{arterial}$ Portal HTN Related SAAG > 1.1	↑σ_{int} or K Non-Portal HTN Related SAAG < 1.1
Cirrhosis	Cancer
R-sided CHF	Peritoneal TB
Budd-Chiari	Nephrotic Syndrome
Portal/Splenic Thrombosis	Protein-Losing Enteropathy
Schistosomiasis	Post-Op Lymphatic Leak
	Bowel Obstruction

Cirrhosis Ascites Therapy	Na < 2g/day H_2O < 2L/day Diuresis with spironolactone 100, Lasix 40 Tap 4-6L off requires Albumin infusion TIPS ↑ blood flow, ↑NH_4, ↑Asterixis, AMS (should not be used for ascites)

Function	Effect of Cirrhosis
Bilirubin	Jaundice, Scleral Icterus, Dark Urine
Bile	Pruritus
Coagulation	**Bleeding** = ↑**PT**, ↑**PTT**, ↑ INR (coags)
Protein	**Hypoalbuminemia** ↑Ascites, Edema
Blood Flow	**Porto-caval shunt, Ascites** (hemorrhoids, caput,

(Portal HTN)	esophageal varices)
Estrogen	**Gynecomastia,** Palmar Erythema
Nitrogen	Asterixis and AMS/Coma

- Some people get **diuretics** (high dose spironolactone and furosemide).
- ***To treat the symptoms of distention,*** repeated **therapeutic paracentesis** can be performed.
- A **TIPS** procedure can relieve ascites, but because of the risk of ***hepatic encephalopathy*** it's often avoided except in treatment of refractory varices.
- Treatment or vaccination against any Hepatitis virus is critical.
- The patient must **stop drinking alcohol.**
- Finally, avoid **NSAIDs,** as they may ↓ ***GFR and ↓ Diuresis.***


1st Presentation OR Fever
? Every Hospitalized Pt with Ascites
TAP
⊕ Cx
>250 PMNs
SBP
Ceftriaxone
(FQ)
PPX with FQ or
Bactrim DS
Polymicrobial
>250 PMNs
Secondary SBP
Ceftriaxone
+
MTZ
Imaging ± Ex-Lap
⊖ Cx <250 PMNs
Sterile
Treat Ascites

Laboratory	Findings
AST/ALT	Moderately Elevated in smoldering dz Normal or Low in cirrhosis
Alk Phos	Moderately Elevated in smoldering dz Normal or Low in cirrhosis
Coags	**↑INR** deficiency of 2,7,9,10
Platelets (CBC)	**Thrombocytopenia most sensitive test**
Total Protein	**Low total Protein – synthesis failure**
Albumin	**Low Albumin** –synthesis failure

U/S	**Nodules, Vein Patency, Fatty Liver** strongly indicative of cirrhosis or not
CT Scan	**Nodules, Masses,** and Ascites, even low amount undetected by U/S or physical
Biopsy	**Definitive Diagnosis** by histologic confirmation, evidence of underlying etiology, specimen for analysis

Varics		HCC	
Path:	Portal-Caval Esophagus	Path:	Cirrhosis Hep B
Pt	Asx Screen Vigorous Bleed	Pt:	ASx screen
Dx:	EGD	Dx:	U/S + AFP q6mo Triple Phase CT
Tx:	Banding (acute) Nadolol (chronic)	Tx:	Resection Transplant RFA, TACE
F/u:	TIPS (encephalopathy)		

Path:	Ammonium	Path:	Strep Gram Neg Rods
Pt	AMS Asterixis	Pt:	Anx Fever, Abdo Pain
Dx:	Clinical	Dx:	Paracentesis > 250 Polys
Tx:	Lactulose Rifaximin Zinc	Tx:	Ceftriaxone
F/u:	TIPS (encephalopathy)	PPx:	FQ or TMP – SMX if SBP or TP < 1.0

Spontaneous Bacterial Peritonitis (SBP)

- A whole bunch of fluid sitting in the abdomen is a nidus for infection.
- So the first step is **rule out infection** - **especially in a first time case or a return with fever.**
- Do a paracentesis and get a **cell count** and **Gram Stain / Culture / Sensitivity.** The cutoff is **250** cells; 250 neutrophils to diagnose SBP. No introduction site may be present (why it's called spontaneous) and it's usually **70% GNR** (E. coli, Klebsiella), sometimes **30% GPC** (Strep pneumo).
- Treat with **ceftriaxone** for double coverage (**fluoroquinolone** ok if pen allergy) and **prophylax** wit **fluoroquinolone**.
- Since this disease can go from asymptomatic to fatal rather quickly, tap all hospitalized patients with ascites.
- The MELD goes up, tap.
- The patient has a fever, tap.
- The patient has pain, tap.
- If the tap is done and finds 250 polys, make the diagnosis of SBP. BUT, if the tap then comes back **polymicrobial,** it means the diagnosis is actually a **secondary bacterial peritonitis** (NOT spontaneous) with inoculation from visceral organs.
- In this case it's necessary to add **metronidazole** to ceftriaxone to cover anaerobes.
- Go find the perforation with an **Ex-Lap.**
- The risk of SBP increases with a Total Protein < 1.0 in fluid, so put these patients on prophylaxis.
- If **they've had SBP** they get fluoroquinolone prophylaxis.
- If they haven't had SBP, but **total protein is <1.0,** they get fluoroquinolone prophylaxis.

Other complications of Cirrhosis

- Varices can bleed.
- Screen for them with an **EGD.**
- Use **nadolol** or **propranolol** as an outpatient.
- If they bleed, they must be banded to stop the bleeding.
- Also give **ceftriaxone** and **octreotide.**
- **Hepatocellular Carcinoma** is screened **q6month.**
- Obtaining a **RUQ Ultrasound** and **AFP** will likely alert/flag the potential diagnosis.
- A **triple phase CT scan** is sufficient to diagnose HCC - **no biopsy** is needed.

- **Hepatic Encephalopathy** is treated with **lactulose**. A patient with hepatic encephalopathy has altered mental status, asterixis, and cirrhosis. ***Backup medications are rifaximin and zinc.***
- **Hepatorenal syndrome** is fatal. Treat a patient with renal failure and cirrhosis by holding the diuretics, **giving albumin** and then **octreotide**.

CIRRHOSIS ETIOLOGIES

Wilson's Disease (Cu)

- Wilson's is a genetic disease of **copper excretion** resulting from a defective transport in the biliary system.
- It prevents extrusion of copper, which results in **copper retention**.
- Copper gets deposited in the liver (**cirrhosis**), basal ganglia (**chorea**) and eyes (the **Kayser-Fleischer** Rings).
- Copper studies will show a ↓ **Serum Ceruloplasmin** (it's all bound up trying to decrease the serum copper) and an ↑**Urine Copper**.
- Serum copper is useless.
- Performing a **slit-lamp exam** on the eyes will show the rings and is ***diagnostic***.
- ***Confirmation*** requires a **Liver biopsy** showing > 250ugCu/g Liver Dry Weight.
- The goal is to get the copper out so use **penicillamine** to chelate Cu and excrete it in the urine.
- Transplant is curative of cirrhosis and Wilson's.

Cirrhosis Etiologies	***AST/ALT in the 1000s:***
Viral	Autoimmune Hepsitits
Wilsons	Acetaminophen Toxicity
Hemochromatosis	Aflatoxin (rare)
Alpha-1 Anti trypsin Deficiency	Actue Viral Hepatitis (A, B)
Primary Sclerosing Cholangitis	Budd-Chiari
Primary Biliary Cirrhosis	
Ethanol	
NASH/NAFLD	
Something Rare	

Patient has...	***Key facts and Diagnosis***
Cirrhosis and COPD	A1-AT deficiency Get a biopsy = **PAS + Macrophages**
Cirrhosis, Diabetes, Tan Skin	Hemochromatosis Get a **ferritin** (very high) or **transferrin** then get a **biopsy** Transplant cures the cirrhosis, not the Hemochromatosis
Cirrhosis, Chorea, and the "eye"	**Wilson's Disease** Start with a **slit lamp** (Kayser-Fleischer) Do NOT get Serum Copper - this is wrong Either **ceruloplasmin** or **urine copper** Transplant cures cirrhosis and disease
Cirrhosis and Inflammatory Bower Disease	**Primary Sclerosing Cholangitis** Start with an **MRCP** Biopsy / ERCP is NOT needed Do **NOT STENT** - ursodeoxycholic acid Can recur in transplant
Cirrhosis and alcohol consumption	**Alcoholic cirrhosis** Stop drinking alcohol Transplant curative
Cirrhosis and positive serology	**Viral hepatitis** Treat Hep B, Treat Hep C Vaccinate against A and B
Cirrhosis and a long list ensuring everything is negative	**NASH** Diagnosis of exclusion Treat symptoms and transplant

Serology	Diagnosis on the TEST
ANCA	PSC
AMA	PBC
ANA	Nothing... Don't be fooled
Ceruloplasmin	Decreased in Wilson's Disease
Ferritin	Elevated in Hemochromatosis
Hep B, Hep C	Viral Hepatitis
Smooth Muscle	Autoimmune Hepatitis
Anti-LKM	Autoimmune Hepatitis

Hemochromatosis (Fe)

- A disease of **Iron Absorption**.
- There's no "off" signal and the gut absorbs all iron.
- The classic triad is **"Bronze Diabetes"**: **Cirrhosis, Diabetes,** and **Hyperpigmentation**.
- While a **transferrin** (>60% men, >50% women) is most sensitive, it's common to start the diagnosis with **Ferritin** (very elevated) and confirm it with a **liver biopsy**.
- The goal is to eliminate iron so chelate it with **deferoxamine** or **serial phlebotomy** titrating to an Fe sat <30 or ferritin < 50.
- Transplant cures the cirrhosis but not the Hemochromatosis.
- ***"Black Liver on MRI."***

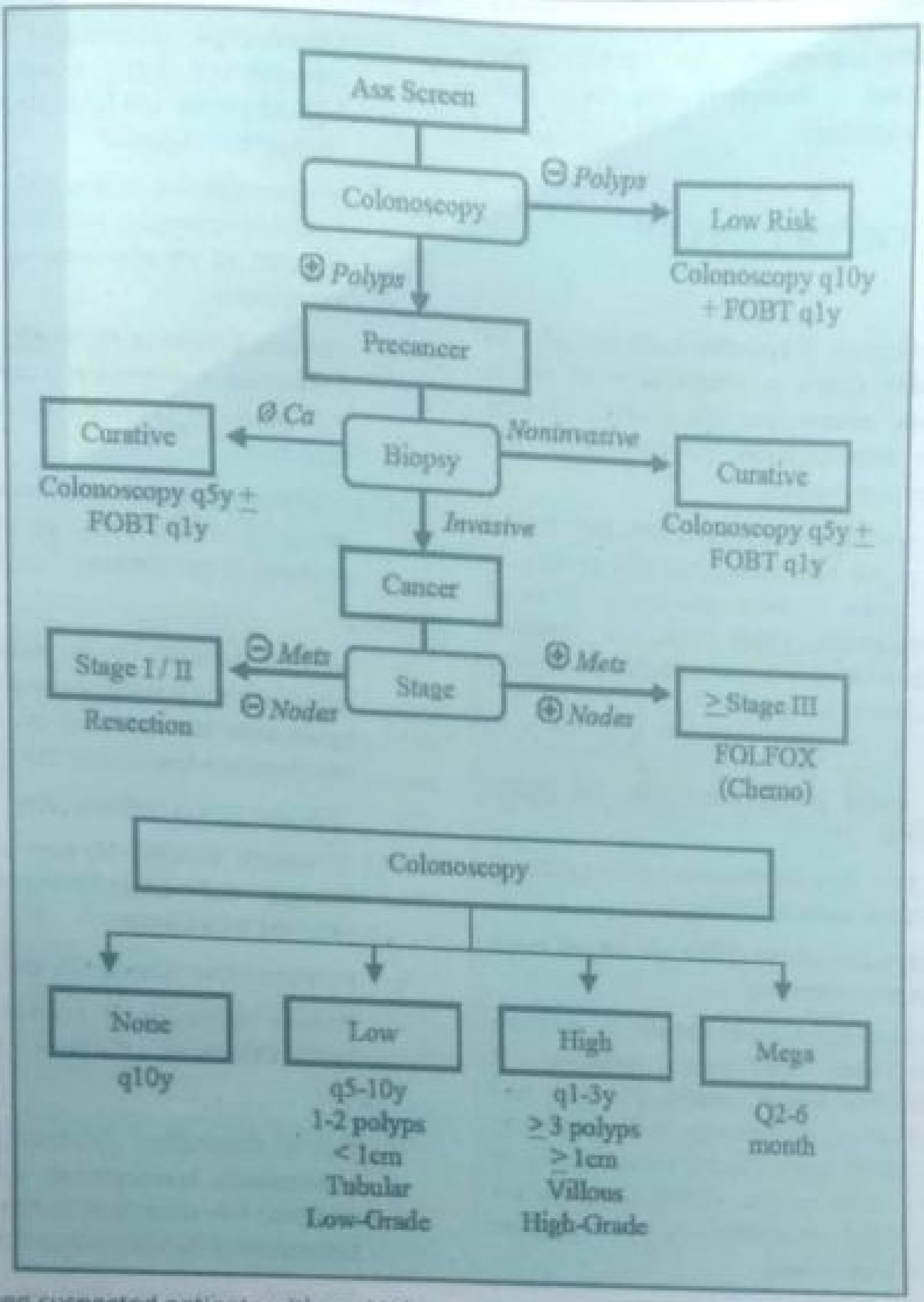
Disease	Presentation	Pathology	Treatment
Familial Adenomatous Polyposis (FAP)	1000 polyps by 18, Cancer by 40, Death by 50	APC gene Mutation	PPX Colectomy
Hereditary Nonpolyposis Colorectal Cancer (HNCC)	3 family members 2 generations 1 under 50 Colon Cancer AND reproductive organs	DNA Mismatch Repair	↑ Screening Start at 20. Or 10 years prior to first CRC
Turcot	GI tumors and Brain Tumors Turcot, Turban (head)		
Gardner	GI Tumors + Jaw Tumors		
Peutz-Jeghers	Nonmalignant polyps and hyperpigmented buccal mucosa + small intestine tumors (hamartomas)		

α1-Antitrypsin Deficiency

- These patients have a mutation in a protease inhibitor that prevents release of α1-AT from the liver. It results in junk accumulating in the liver (**cirrhosis**) and overactive elastase in the lungs (**emphysema**).
- To confirm, take a **biopsy** and see the PAS **Hepatocytes** or do PCR + phenotyping.
- **PiZZ** is the worst phenotype, while **PiMM** is normal. Since the problem is with the liver a **transplant** is **curative**. **α1-AT replacements** will help the emphysema but not with the cirrhosis.

Primary Sclerosing Cholangitis

- An **autoimmune disease** that affects **males** and causes fibrosis of **extrahepatic ducts** (macroductal disease).
- There's a high association with **Ulcerative Colitis.**
- It presents with an obstructive picture of the biliary system that may involve the pancreas.


Asx Screen
Colonoscopy
⊖ Polyps
Low Risk
Colonoscopy q10y
+ FOBT q1y
⊕ Polyps
Precancer
Ø Ca
Curative
Colonoscopy q5y ±
FOBT q1y
Biopsy
Noninvasive
Curative
Colonoscopy q5y ±
FOBT q1y
Invasive
Cancer
⊖ Mets
⊖ Nodes
Stage I / II
Resection
Stage
⊕ Mets
⊕ Nodes
≥ Stage III
FOLFOX
(Chemo)
Colonoscopy
None
q10y
Low
q5-10y
1-2 polyps
< 1cm
Tubular
Low-Grade
High
q1-3y
≥ 3 polyps
≥ 1cm
Villous
High-Grade
Mega
Q2-6
month

- Screen suspected patients with an **ANCA**.
- The **MRCP** is essentially diagnostic, showing a **"beads on a string"** pattern.
- **ERCP and biopsy** is **NOT required**, but will show **onion-skin fibrosis** if performed.
- **Do NOT** place a stent to alleviate obstruction (it just makes transplant harder) though symptoms should be treated with cholestyramine or **ursodeoxycholic acid**.

Primary Biliary Cirrhosis

- An **autoimmune disease** that affects **females** and causes fibrosis of **intrahepatic ducts** (microductal disease). Since these are small structures MRCP will look normal.
- Patients are otherwise **asymptomatic young women** with cirrhosis.
- Screen with an **AMA, confirm with a biopsy.**

- Immunosuppression to start, then transplant – though it may recur even after transplant.

COLON CANCER

Pathogenesis

- Colon cancer is typically a disease of **> 50 yr olds** that's a progression of either **genetic errors** (see the chart) or **long term inflammation** (Crohn's, UC) into cancerous growth.
- **The mechanism is important, but there's loss of the APC, ATM, and p53 genes - in that order - that eventually turns a premalignant polyp** into an **invasive carcinoma**. The process (polyp à Cancer) occurs over 3-7 yrs.

Patient

- The initial presentation can be highly variable.
- The best way to discover colon cancer is with **appropriate screening**.
- ***Think colon cancer if you see any of these three presentations.***

  1. A post-menopausal female or any male with **Iron Deficiency Anemia,** 2 **alternating bowel habits** (diarrhea and constipation) with **change in the caliber of their stool** (generally to "pencil thin"), or finally, there may be nothing to tip you off - the initial presentation is 3 a **metastasis** to the **liver** or **lung.**

Screening

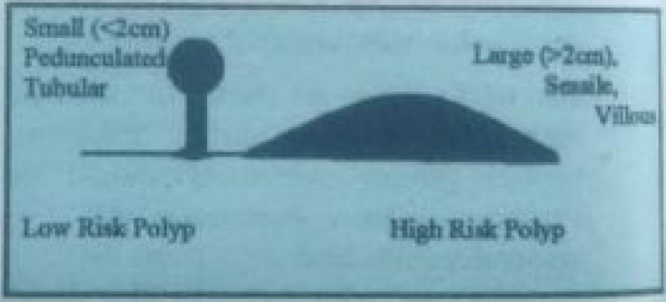
- **Colonoscopy** is the golden standard done **q10y** unless abnormalities are found, at which the frequency is increased. This will identify **adenomatous polyps** which will be removed and analyzed.
- **Sessile, Villous** polyps have an increased risk of malignant transformation, while **pedunculated, tubular** polyps have a lower risk.
- Colonoscopy is required in order to visualize the entire colon because only 50% of polyps are Left sided (opposed to rigid sigmoidoscopy).
- In communities where colonoscopy isn't available screening with **FOBTx3 annually** or **FOBT q3 yrs with Flex Sig q5yrs** is also appropriate.
- Barium Enema is ***NOW NEVER the right answer as it only detects colon cancer or ≥ Stage III disease (incurable with resection).***
- If either the barium enema or the flex sign are positive a colonoscopy must be done anyways to get a biopsy.

Diagnosis

- In someone with severe disease all that's necessary is a **barium enema** to reveal the **apple core lesion** (don't do it, but still a test question because of the radiograph).
- The best test is **colonoscopy.**
- If there's invasive disease a **metastatic workup** (CT chest/abdomen/pelvis) is required for **staging.**
- Intraoperative staging can be performed.
- Disease regression or relapse is followed by the **CEA levels** – it's never diagnostic.

Treatment

- This is dependent on staging. If there's **extracolonic involvement** (Lymph Nodes or Mets) the treatment is **FOLFOX** (5-Fu + Leucovorin + Oxaliplatin) or **FOLFIRI.**
- Recently added to improve remission is **Bevacizumab, a VEGF Inhibitor.**
- If there's no extracolonic involvement a simple resection is curative.



DIVERTICULAR DISEASE

rticulosis

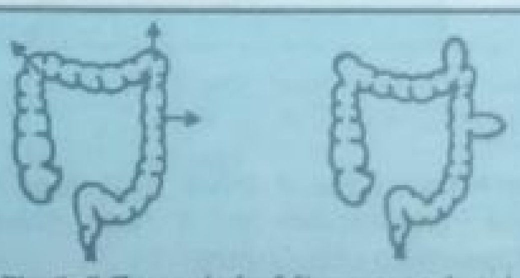
- Diverticulosis is the actual pocket - the physical outpouching of the colon caused by ↑ **luminal pressure** inside it.
- It's typically the result of a diet rich in **red meat** and **deficient in fiber**.
- Repeated constipation causes the colon to contract against hard stool, resulting in ↑ pressures and eventually **outpocketing** of the colonic mucosa. It's a very common condition in the United States that's **asymptomatic** and often an incidental finding on routine screen.
- By eating a higher fiber diet and reducing red meat the **disease and its complications** (conditions listed below) **can be prevented**.
- Diverticuli are typically a disease of the **elderly** (> 50 yr). They occur more often on the **left than the right** because stool is ***harder on the left.***
- They can be an incidental finding on CT scan, but are definitely diagnosed by **colonoscopy**.

rticular Spasm = Symptomatic uncomplicated rticulosis

- This is caused by a spasm of the diverticulum - especially when diet hasn't been changed.
- It will present as an **LLQ postprandial pain** that's **relieved** by a **bowel movement**.
- The question stem will read like IBS but in an elderly patient.
- It's treated with a **high fiber diet** to prevent future spasms.

rticular Hemorrhage

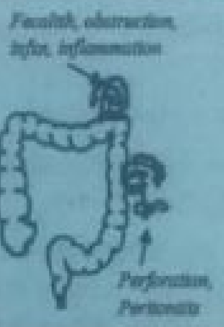
- An arteriole in the dome of the diverticulum gets stretched, tears, and bleeds. This presents as a **brisk, painless bleeding** per rectum.
- It isn't the FOBT of Iron Deficiency Anemia slow bleed – it's a severe GI bleed with rapid blood loss.
- It'll be diagnosed by first ruling out an upper GI Bleed (**NG Tube / EGD**) and found either on **colonoscopy, tagged RBC scan**, or **Angiogram** .
- Diverticuli bleed from the right colon more often than the left (but diverticula occur on the left more than on the right).



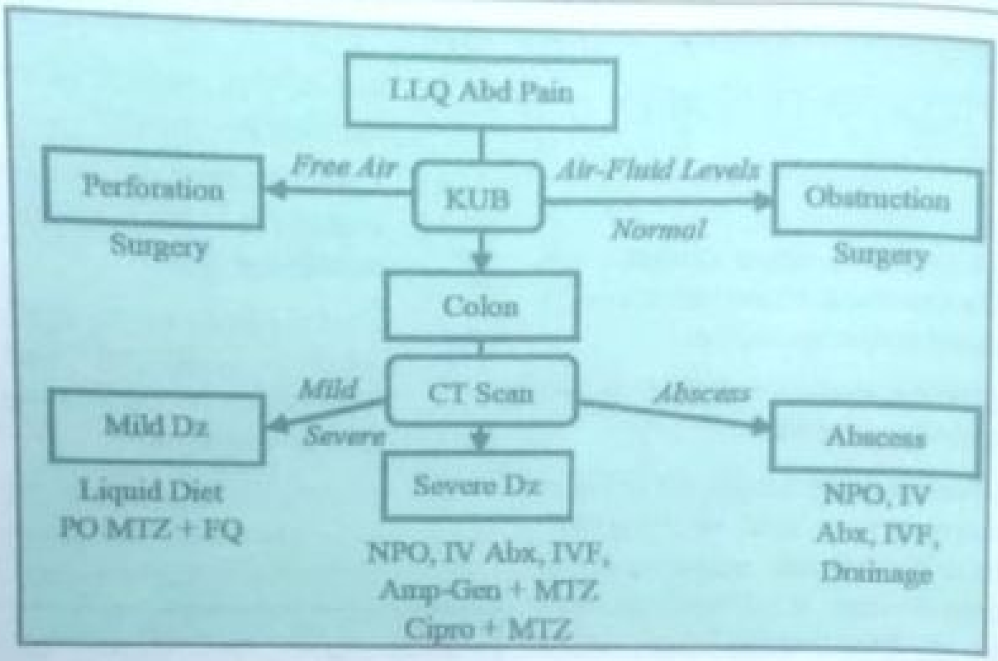
***Diverticuli.** The normal colon (left) generates intraluminal pressures (the arrows) as a result of low fiber and chronic constipation. At select locations, the wall of the colon protrudes, stretching the mucosa (right)*

Spasm:
Px: Diverticulosis + Continued Poor Diet
Pt: Elderly pt + LLQ post prandial pain
relieve with BM
Dx: Clinical, Severe disease r/o
Tx: High Fiber Diet

Hemorrhage
Px: Arteriole at the dome of diverticuli tears
Pt: Elderly bright red blood from rectum
Dx: (1) r/o UGIB w/ NGT + EGD
(2) Colonoscopy (Ø Bleeding)
Arteriogram (Brisk Bleeding)
Tagged RBC (Slow Bleeding)
Tx: Embolization, Cautery, Resection



Diverticulitis
Px: Diverticulitis + Fecalith ± Perforation
Pt: LLQ Pain in an elderly pt w/ acute onset
and mild to severe fever + leukocytosis
Dx: (1) r/o Perforation/Ileus with KUB
(2) CT Scan for severity
(3) Avoid Colonoscopy
Tx: Mild = PO FQ + MTZ + Liquid Diet
Severe = NPO, IVF, IV Abx
Abscess = Drainage
Refractory = Colectomy


LLQ Abd Pain
Free Air
KUB
Air-Fluid Levels
Perforation
Surgery
Normal
Obstruction
Surgery
Colon
Mild
CT Scan
Abscess
Mild Dz
Severe
Abscess
Severe Dz
Liquid Diet
PO MTZ + FQ
NPO, IV Abx, IVF,
Amp-Gen + MTZ
Cipro + MTZ
NPO, IV
Abx, IVF,
Drainage

Diverticulitis

- Diverticulitis has a similar pathogenesis and presentation as a **Left Sided Appendicitis** of the **elderly**.
- A fecalith forms across a diverticulum causing obstruction, inflammation, and the compromise of the blood supply to the diverticulum. This results in **infection**, **inflammation**, and **perforation**.
- The presentation is highly variable - from a **mild inflammation** (low fever, mild leukocytosis, and abdominal tenderness) to **florid peritonitis** or perforation (high fever, massive leukocytosis, rebound, guarding).
- Diagnosis is made by first ruling out a surgical emergency with a **KUB** to ensure no free air or ileus, then via a **CT scan** to identify the extent of the disease.
- **Avoid Colonoscopy** until 2-6 wks after acute disease has resolved (to minimize the risk of perforation).
- Treatment is dependent on the severity.
- **Mild Dz** is treated with oral antibiotics and adequate bowel rest (liquid diet only).
- In more **severe disease** use **NPO**, **IVF**, and **IV Antibiotics.** Multiple combinations are acceptable as long as they get gram negatives and anaerobes (**Ampicillin, Gentamicin and Metronidazole, Ciprofloxacin and metronidazole,** Or **pip/tazo**).
- If there's an abscess on the CT it needs to be **drained**.
- Finally, colectomy is indicated in **severe** or **refractory** disease.

ESOPHAGITIS

Introduction

- If a patient presents with **Odynophagia, dysphagia,** or **chest pain,** one consideration should be an inflammation of the esophagus.

Causes of Esophagitis = "Piece of Esophagus"	
Pill Induced	NSAIDs, Abx, NRT
Infections	HIV, CMV, Herpes, Candida
Eosinophilic	Asthma, Eczema, Food Allergy
Caustic	Alkali (Drain Cleaner), Acid
Everything else	GERD, Rare cause

Pill-Induced Esophagitis

- Prolonged direct exposure of the esophagus mucosa cause erosive esophageal ulcerations.

- Some drugs are notorious: **NSAIDs, Anti-retrovirals**, and **Antibiotics** (Doxycycline, Clindamycin, Sulfamethoxazole/Trimethoprim aka Bactrim) - especially the cheaper, non-enteric coated pills.
- Because it's a direct result of constant exposure, patients should take pills with **4oz H2O** and while **erect and upright**.
- After exposure occurs **endoscopy** can reveal and allow removal of the tablet or pill, but it takes time to heal after pill removal.

Infectious Esophagitis

- Infections of the esophagus aren't common.
- The patient must have a **risk factor** that makes them **immuno-suppressed** such as: organ transplant, leukemia or lymphoma, steroids, or **HIV/AIDS**.
- Concurrently, they'll get **opportunistic infections** like **candida, HSV**, and **CMV**. While an **Endoscopy** with **Biopsy** is needed to get a definitive diagnosis, certain physical findings can enhance the chances of pre-procedural diagnosis.
- **Oral ulcers** (herpes labialis) are linked to **Herpes** while **thrush** is associated with **Candida**.
- Treatment for the infections is dependent on the infectious agent (see the chart).

Bug	*Finding*	*Treatment*
Candida	Thrush	Nystatin and Fluconazole
Herpes	Oral Ulcers	(Val) Acyclovir or Foscarnet
CMV	-	(Val) Ganciclovir or Foscarnet
HIV	AIDS	HAART

Eosinophilic Esophagitis

- This is an allergic reaction in the esophagus.
- Look for the history of Asthma, Atopy, and Allergies with Esophagitis.
- Get an **endoscopy with biopsy** showing **eosinophilia** (>15/hpf).
- Even if you see the eosinophils, treat it like GERD with **PPI**.
- If PPI fails, then use **swallowed aerosolized steroids**.

Caustic Esophagitis

- Caustic Esophagitis is Either accidently (**children**) or purposefully (adult **suicide**) drinking caustic substances (i.e. **alkali-like** lye, drain cleaner, or any **acid**) ruins the esophagus.
- The burning of the esophagus produces **chest pain + odynophagia**, leading to the avoidance of swallowing, resulting in **drooling**.
- Burning of the larynx causes **stridor** or **wheezing**.
- The first thing to remember is that one should **NEVER** induce vomiting to expel a caustic ingestion.
- An **endoscopy** is done within 24 hrs to evaluate the severity.
- **Low Severity** (edema, erythema, shallow ulcers) can be moved from liquid to solid diet in the first 24-48 hrs.
- **High severity** (deep ulcers, circumferential burns, black necrosis) has a high incidence of **perforation, bleeding, strictures**, and **fistulas** so must remain NPO for 72 hrs, with constant monitoring for the development of complications. 70% develop strictures while 2-3% develop cancer (surveillance required 15-20 years later).

Diagnosis	*Review*
Pill Induced	Pt: NSAIDs, NRTs, Abx (clinda, doxy, Bactrim) Dx: Endoscopy Tx: Pill removal, time, PPIs for comfort PPx: Enteric Coating, Erect

	Ingestion, 4oz H20
Infectious	Pt: Immunocompromised, Thrush, Ulcers Dx: Endoscopy with Biopsy Tx: Cause dependent, Antifungal, Antiviral
Eosinophilic	Pt: Child with Asthma, Eczema, Odynophagia Dx: Endoscopy with Bx shows Eosinophilia Tx: Remove foods then reintroduce, PPIs
Caustic	Pt: Children (accident) Adult (suicide) ingestion of caustic alkali or acid, presenting with drooling, odynophagia Dx: endoscopy within 24 hrs Tx: High Severity: NPO x 72 hrs (risk perf) Low Severity: Liquid → Solid w/i 48 hrs
Everything Else	Consider GERD, cancer, other mechanical/motility disorders

ESOPHAGUS

Introduction

- The purpose of the esophagus is to carry food from the mouth to the stomach - AKA **swallowing**. So it's no surprise that disorders of the esophagus present as **dysphagia** (difficulty swallowing) or **odynophagia** (pain on swallowing).
- An important initial step is to separate the **motility/functional** dysphagia from the **mechanical/obstructive** dysphagia.
- The former is dysphagia to everything at once, while the latter is dysphagia **progressive from foods to liquids**.

MOTILITY

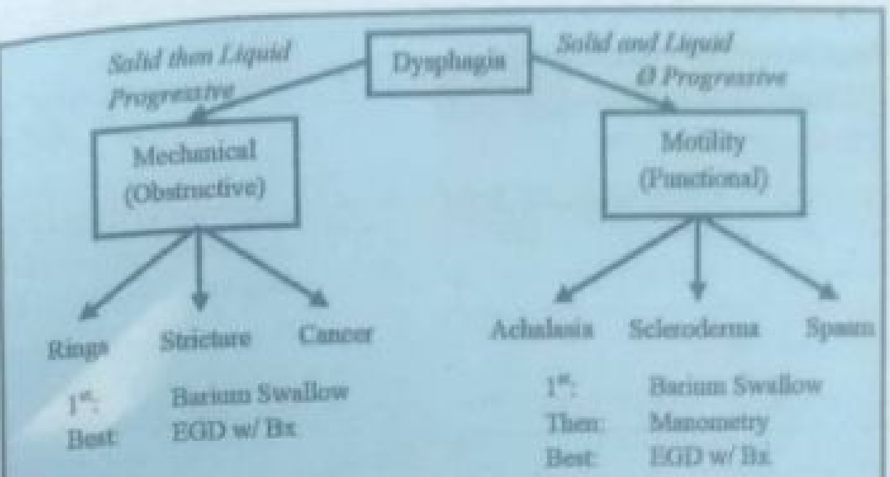
Achalasia

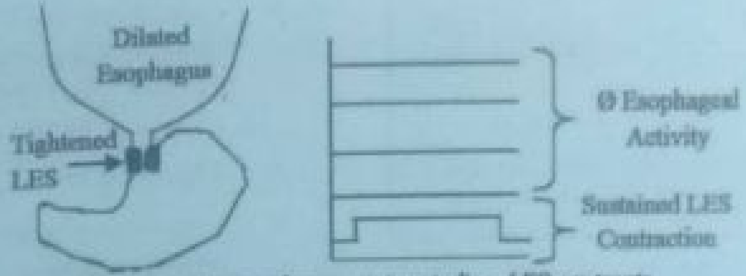
- This is a failure of the **LES** to relax and presents as dysphagia to solids and liquids.
- Food enters the esophagus, moves just fine to the stomach, but can't fit through a tightened LES.
- Patients describe a **knot** or **ball of food** behind their sternum along with dysphagia.
- A diagnosis can be made on **barium swallow**, demonstrating a **bird's beak**.
- It's confirmed with a **manometry** that shows hyperactive contraction and inactivity of the rest of the esophagus.
- An EGD must be done to rule out cancer **(pseudoachalasia)** and to reveal the **absent myenteric plexus**.
- For treatment, the LES has to be opened.
- Botulinum must be repeated and is used for poor surgical candidates.
- Dilation carries perforation risk. The preferred treatment is **myotomy.**

Scleroderma

- Scleroderma is an autoimmune disorder of **collagen deposition**.
- Whether CREST or Systemic Sclerosis, collagen in the esophagus means the LES cannot contract.

- The patient will present with **relentless GERD.**
- A definitive diagnosis is made with **manometry** showing a **relaxed esophagus** (tone) and **↓pressure** in the **LES.** Treat symptomatically with **PPIs.**

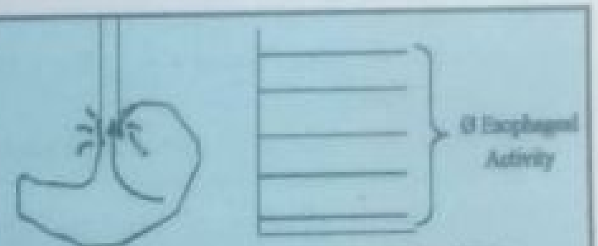

Dysphagia
Solid then Liquid
Progressive
Solid and Liquid
Ø Progressive
Mechanical
(Obstructive)
Motility
(Functional)
Rings
Stricture
Cancer
Achalasia
Scleroderma
Spasm
1st: Barium Swallow
Best: EGD w/ Bx
1st: Barium Swallow
Then: Manometry
Best: EGD w/ Bx


Dilated
Esophagus
Tightened
LES
Ø Esophageal
Activity
Sustained LES
Contraction

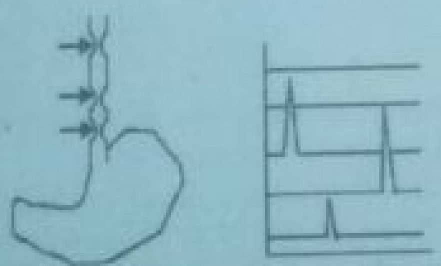
Achalasia depiction and manometry studies. LES contracts as normal but cannot relax, producing sustained contraction.

Esophageal Spasm

- This looks like an MI at first glance.
- It presents with a crushing, retrosternal chest pain that's **relieved with nitrates** but isn't an MI.
- On first presentation, rule out MI with ECG and troponins.
- Thereafter, esophageal spasm is diagnosed by **manometry** showing **erratic, diffuse spasm** unrelated to eating, drinking, or position.
- A **barium swallow** done at the time of pain may show multiple regions of spasm, the **"corkscrew esophagus"** (though it will be normal if not experiencing pain).
- Treat this with **Calcium Channel Blockers** or **Nitroglycerin** as needed.


Ø Esophageal
Activity

***Scleroderma** depiction and manometry studies. LES is persistently relaxed permitting regurgitation of acid contents. LES has no activity at all.*

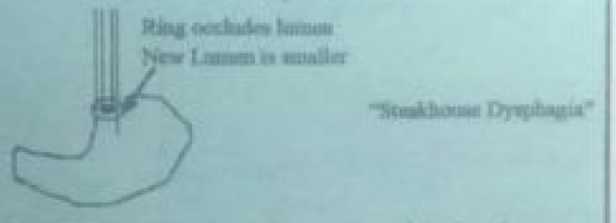


***Esophageal Spasm** depiction and manometry. Diffuse, uncoordinated, painful contractions of the esophagus.*

MECHANICAL

Schatzki Ring

- A **fibrous ring** located at the LES causes only **large diameter** foods to get stuck.
- This will be a very **episodic** (months in between) **dysphagia** with **odynophagia**.
- Since most food is cut or chewed well they'll get by the ring.
- Only once every so often does the food get stuck - hence **episodic**. A **barium swallow** will show a narrowed lumen and an **EGD** will yield definitive diagnosis with visualization and biopsy.
- Breaking the ring will alleviate symptoms.



Schatzki Ring depiction. Only once in a while does large caliber food get stuck. Thus, it is the critical diameter food that makes this disease

Plummer-Vinson Syndrome

- **Esophageal Rings** + **Esophageal Webs** + **Iron Deficiency Anemia**, typically in a woman, is Plummer-Vinson.
- Note that these patients have a special type of ring located in the **upper esophagus**.
- They also have an ↑ risk of **squamous cell carcinoma** of the esophagus.
- There's no treatment but the patient needs screening EGDs to screen for cancer.
- Prophylactic esophagectomy is NOT indicated.

Stricture

- Potential consequences of long-standing GERD is Barrett's and Cancer.
- Another, considered **grade 4 GERD**, is a stricture.
- So much inflammation over such a long period causes scarring.
- Another cause of stricture is **caustic ingestion** (harsh acid or base).
- The scarring **enters the lumen.** This is a **progressive history of GERD** or remote history of ingestion followed by motility dysphagia.
- There may be weight loss (b/c they can't eat as much, distracting you towards cancer).
- Diagnosis is initially made with a **barium swallow** then confirmed by **EGD with Biopsy** for definitive diagnosis.
- Treatment is the aggressive management of GERD (high dose PPI) and **resection** of the stricture.

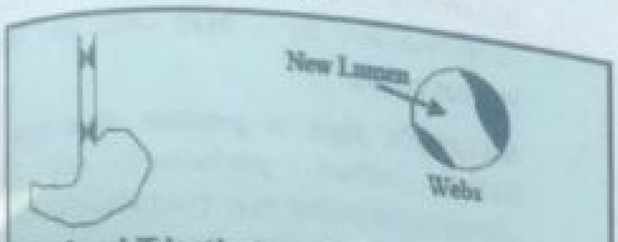
Cancer

- Cancer presents as **progressive weight loss** and **progressive dysphagia** in an older **person** with **GERD** (adenocarcinoma) or in a **smoker/EtOH** (squamous cell).
- There's often an associated **weight loss**.
- ***Progressive = obstructive, weight loss = cancer, risk factors = which cancer.***
- A **barium swallow** is done first to identify the area of the lesion and to rule out cancer high in the esophagus (which might perforate if an EGD is done first).
- Follow up the swallow with an **EGD** and **Bx**.
- *If positive*, **stage** with a (PET)**CT**.
- **Resection** and **chemo** is the treatment as most of the cancers are **invasive** at the time of diagnosis. Because acid refluxed from the stomach into the bottom of the stomach, **adenocarcinoma** is at the ↓**1/3** of the esophagus. Because smoke and hot drinks enter at the top of the esophagus, **squamous cell** is at the ↑**1/3**.

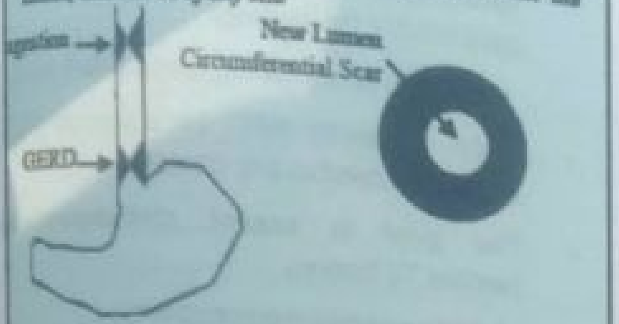
Zenker's

- In a **really old guy** with **bad breath** who has trouble eating (**coughing + gurgling** at the start of eating) suspect a Zenker's diverticulum.

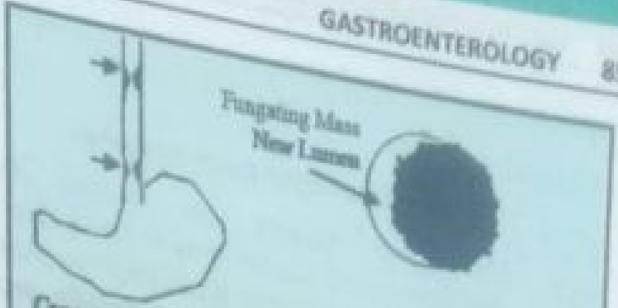
- The diagnosis is sealed if the patient **regurgitates undigested food** days after eating it.
- The diverticulum is a **false** diverticulum caused by **decades** of ↑ **pressure**.
- Do a **barium swallow** to identify and an EGD if need be.
- Treat with resection.



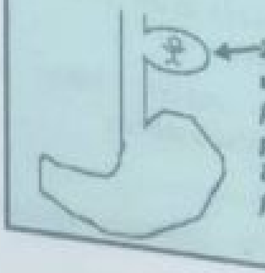
Esophageal Webs side view and cross-section. Webs can occur anywhere in the esophagus. They stay within the lumen, and can be of any size



Stricture side view and cross-section. GERD causes stricture at lower esophagus, ingestion can be anywhere, usually at entrance. Scar is circumferential with a new, smaller lumen in the center



Cancer side view and cross-section. GERD causes adenocarcinoma in the distal esophagus. Toxic exposure causes squamous cell in the proximal esophagus. Fungating mass eats into the lumen from a single focus, new lumen is oddly shaped. This tumor is depicted as having invaded the wall of the esophagus.



Zenker's. False lumen with an undigested stick figure in it. This figure will leap out at night onto the pillow. It will first make this old man's breath smell terrible and it'll be hard for him to eat.

Disease	*Presentation*	*Classic Sxs*	*1st Test*	*Best Test*	*Treatment*
Achalasia	Motility	Knot or Ball of Food at esophagus		Manometry	Dilation, Botox, Myotomy
Scleroderma	Motility	CREST, Female			GERD tx, Ø cure
Esophageal Spasm	Motility	CP better with Nitro, CCB			NTG, CCB pm
Schatzki Ring	Mechanical	Episodic to Large caliber foods			Resection
Plummer Vinson	Mechanical	Iron Def Anemia, Webs, Feamle			Ø, Monitor for Cancer
Stricture	Mechanical	GERD with Weight Loss or h/o Caustic Ingestion	Barium Swallow	EGD ⊕ Bx	Resection
Zenker's	Mechanical	Old Man, Halitosis, regurgitation			Resection
Cancer	Mechanical	GERD ⊕ Weight Loss Or Or Smoking + EtOH			Resection ± Chemo

GALLBLADDER DISEASE

Gall Stones

- There are ***two major types of stones.***
- **Cholesterol Stones** are caused by cholesterol and appear green. The person who is at risk for these types of stones are the **"5 Fs:"** ***Fat, Female, Forty, Fertile, and Native American*** (ok, so that last one wasn't an F).
- The other stone is **Pigment Stones** caused by **hemolytic disease**. They're **black in color** and coincidentally occur in **African Americans** more often.
- In reality, most people have a combination, called **mixed stones**.

Cholelithiasis

- When the gallbladder contracts against these stones, it hurts.
- Cholelithiasis is simply the presence of stones in the gallbladder.
- There's no obstruction, inflammation, or risk of death – just pain.
- Gallstones will present with a **Colicky RUQ Pain** that **radiates to the shoulder** made worse by **fatty foods.**
- Eating, and fatty foods in particular, cause the gallbladder to contract.
- Most people who have gallstones **are asymptomatic** and don't **require** prophylactic cholecystectomy.
- Better diet, exercise, and ↓ cholesterol can prevent the stones from **becoming** symptomatic.
- Symptoms arise at a rate of about 30% every 2 years.
- Diagnosis is made with the **RUQ U/S** showing stones in the gallbladder.
- Treat with **cholecystectomy** (surgery) or **ursodeoxycholic acid** for non-surgical candidates.

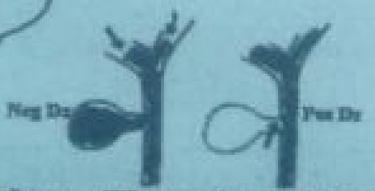
Cholecystitis

- When a gallstone gets stuck in the **cystic duct** an inflammatory process develops in the gallbladder.
- This shifts from the colicky abdominal pain to a **constant RUQ pain.**
- As the name implies, "- itis" means inflammation, and so the pain is often accompanied by a **mild fever** and mild **leukocytosis**.
- ***Murphy's Sign is positive*** (this test is better when performed with an ultrasound probe over the gallbladder).
- **Diagnose** with an **ultrasound** (pericholecystic fluid, gallstones, and gallbladder thickening).
- If the **U/S** is equivocal, use a **HIDA scan.**
- Upon diagnosis **NPO**, **Intravenous** Fluids, and IV antibiotics are started.
- The goal is **urgent cholecystectomy** (within 72 hours).
- Waiting only worsens outcomes.
- **Cholecystostomy** (a tube) is possible for poor surgical candidates, but it's rarely the answer on the test.

Normal Anatomy of the Hepatobiliary system

Asx Gallstones present, without obstruction

Acute Cholecystitis. Gallstone lodges in Cystic Duct, inducing inflammation of the Gallbladder. No hepatic/pancreatic involvement



HIDA scan. Normal on left has tracer throughout biliary system. Obstruction on right prevents filling of the gallbladder. Positive study There is involvement

Dz	Path	Pt	Dx	Tx
Stones ("Lithiasis")	Cholesterol = the "Fs" Pigmented = Hemolysis	ASX	U/S, Diagnosis not required	None
Cholecystitis	Cystic Duct Obstruction	RUQ Pain, Murphy's Sign	U/S → HIDA mild fever, mild leukocytosis	Urgent Cholecystectomy
Choledocholithiasis	Common Bile Duct Obstruction = Hepatitis and/or Pancreatitis also	RUQ Pain, Murphy's Sign + ↑AST/↑ALT, ↑Lipase/↑Amylase	U/S →MRCP mild fever, mild leukocytosis	ERCP, Cholecystectomy
Ascending Cholangitis	All of the above PLUS Infection behind the stone	RUQ Pain, Murphy's Sign + ↑Labs, T >104, Leukocytosis	U/S→MRCP→→ERCP severe fever and leukocytosis	ERCP Emergent Cholecystectomy

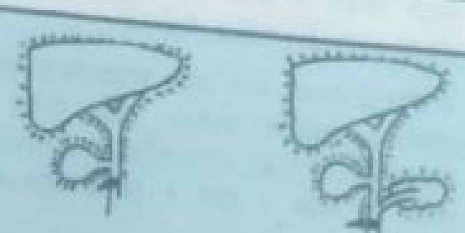
Choledocholithiasis

- A stone in the common bile duct has a number of potential consequences.
- The first, **painful jaundice** is classic for gallstone obstruction of the biliary tree.
- Depending on the severity and location of the stone, stones in the biliary tree can lead to hepatitis or pancreatitis.
- ***Gallstone pancreatitis is the second most common cause*** of pancreatitis in the US. There's often (but need not be) mild inflammation, presenting with low-grade fevers and mild leukocytosis in addition to the symptoms of the associated organs

- Hepatic obstruction = **pruritus, jaundice,** and ↑LFTs.

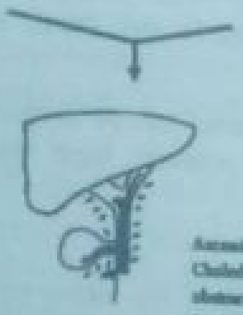
- Pancreatic obstruction = **Pain, N/V, ↑Amylase, ↑Lipase**

- Diagnosis begins with **RUQ U/S** which should show **dilated ducts.**
- If the ducts aren't dilated, but Choledocholithiasis is suspected, do an **MRCP.**



Choledocholithiasis. Obstruction of common duct proximal to pancreas. Pancreas not involved, liver is. ↑AST/ALT, Conj Bili

Choledocholithiasis. Obstruction of common duct distal to pancreas. Both involved. ↑AST/ALT, ↑Conj Bili, ↑Amylase, ↑Lipase



Ascending Cholangitis
Choledocholithiasis + Infxn Proximal to obstruction. Chills, High Fever, Severe Leukocytosis

Charcot's Triad (Cholangitis):
1) RUQ Pain
2) Fever
3) Jaundice

Reynold's Pentad (Cholangitis):
1-3) Charcot's Triad
4) Hypotension
5) AMS

- Treatment is with **ERCP** and stone retrieval.

- Prophylactic antibiotics awaiting the procedure are generally recommended, sticking with the NPO, IVF, IV abx theme for acute disease.
- Eventually a **cholecystectomy** should be performed, but this can be done in the urgent to elective period if an ERCP is done.

Ascending Cholangitis

- Bile stasis is a nidus for infection.
- Most infections of the biliary tree (except when surgical intervention has been performed) will be isolated to gut flora: **E. coli, Klebsiella**, or **Enterobacter**.
- These are gram negative organisms and can present with quite a sick patient.
- The combination of Painful Jaundice + High Fever > 104 °F is **Charcot's Triad** (**RUQ pain, Jaundice, Fever**).
- If the patient has also **hypotension** and **altered mental status**, then they have Reynold's Pentad. Immediate resuscitation with **IV Abx + IVF + NPO** should be performed.
- Diagnosis can be facilitated by **Ultrasound** showing dilated ducts.
- The patient must receive **emergency ERCP** to remove the stone and allow biliary flow.
- **Cholecystectomy** can be performed once the patient recovers from their severe illness.

Antibiotic Choice

- The organisms of the biliary tree are the organisms of the GI tract - primarily Gram Negative Rods and Anaerobes.
- Multiple regimens exist. Ciprofloxacin + Metronidazole, Ampicillin- Gentamycin + Metronidazole, and Pip/Tazo are appropriate.
- Particularly, Pip/Tazo is correct if skin flora must be considered; it's wrong if considering only GI bugs.

GERD

Gastroesophageal Reflux Disease

- GERD is a common disorder of the esophagus that results in esophagitis.
- A **weakened Lower esophageal sphincter (LES)** allows gastric acid to regurgitate and burn the distal esophagus.
- There are ***two types of symptoms***.

  1) Typical (Intestinal) symptoms are a product of acid regurgitation in the esophagus. It predominates with a retrosternal **burning chest pain** that's worse with **spicy foods** and **recumbency**, better with **sitting up, antacids**, and cold water.

  2) Atypical (extra-intestinal) symptoms are a product of acidic damage to the proximal esophagus and airways. In this variant **hoarseness, cough**, and **nocturnal asthma** predominate in symptoms.
- **The first diagnostic step** depends on symptoms. If there are **no alarm symptoms** then ***the first "test"*** is **treat with a PPI and lifestyle x 6 weeks.**
- Lifestyle modifications are variable and have mixed benefit; **initial therapy** must include a PPI.
- **Lifestyle modifications include**

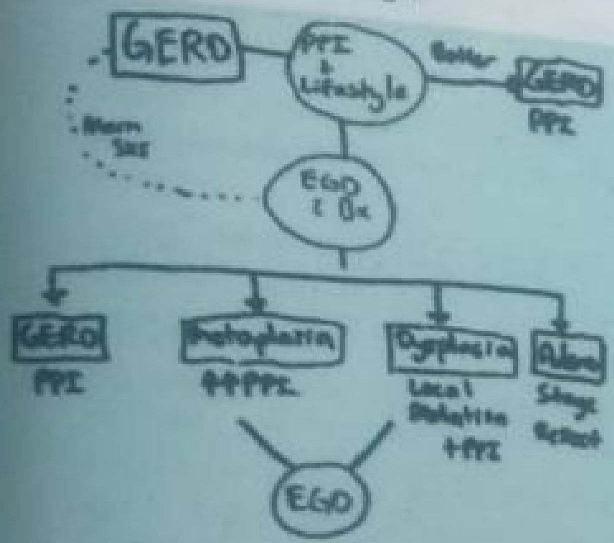
  1) avoiding food hours before recumbency,

  2) small meals,

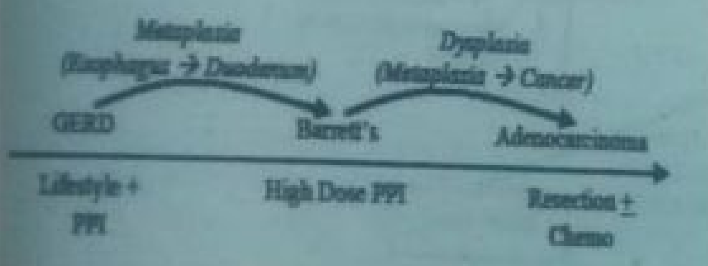
  3) elevating the head of the bed,

  4) avoidance of LES dilators: alcohol, smoking, peppermint, and chocolate.
- If there are **any alarm symptoms** on presentation OR **PPIs fail to resolve** the disease, the next necessary step is **endoscopy with biopsy.**
- **Endoscopy** allows assessment of severity of the esophagitis **(Grade 1 – 4), evaluation for ulceration, and enables** us **to rule out Barrett's and Cancer.**

- The **best test** is **24-hour pH monitoring**, though it is rarely performed.
- If surgical intervention is required for GERD, this test (as well as manometry) should be performed.
- The treatment of the disorder is based on the endoscopic findings.


GERD
PPI & Lifestyle
Better
GERD
PPI
Alarm Sx
EGD c̄ Bx
GERD
PPI
Metaplasia
↑↑PPI
Dysplasia
Local Ablation +PPI
Aden
Stage Resect
EGD

GERD	PPI
Barrett's	High Dose PPI
Dysplasia	Ablation
Adenocarcinoma	Resection


Metaplasia
(Esophagus → Duodenum)
Dysplasia
(Metaplasia → Cancer)
GERD
Barrett's
Adenocarcinoma
Lifestyle + PPI
High Dose PPI
Resection ± Chemo

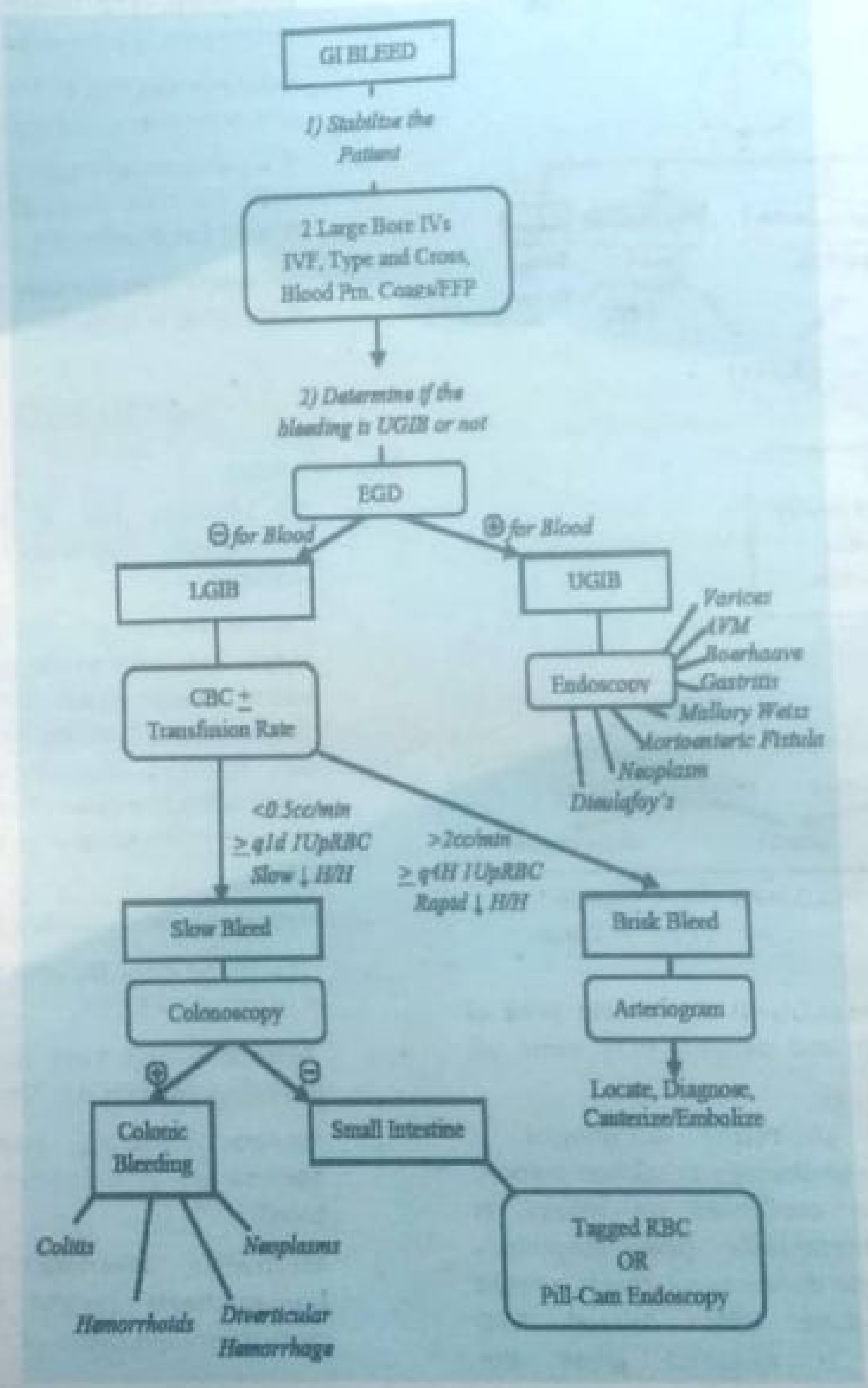
- **GERD** is treated with the **lowest dose of PPI** possible and patients may come off the PPI.
- **Metaplasia** (Barrett's) esophagus is identified on endoscopy as salmon-colored mucosa and confirmed on biopsy as intestinal metaplasia (the esophagus changes to the duodenum). This is treated **with high-dose PPIs.** Annual EGD surveillance is required given the increased risk of adenocarcinoma in Barrett's Esophagus. It can then be spaced out to q3yrs if stable.
- **Dysplasia** is nearing malignancy and treated with **local ablative therapies**. The method is up to the provider: cryoablation, laser ablation, or radiofrequency ablation. This requires more frequent EGD surveillance than Metaplasia. The severity of the dysplasia determines the surveillance rate.
- **Adenocarcinoma** is treated with staging and **resection** vs chemo and radiation.
- If a patient can't tolerate PPIs or doesn't wish to take medications for life, the **Nissen Fundoplication** can be performed.
- Be cautious as this may result in Achalasia if the wrap is made too tight.

GI BLEED

Upper vs Lower

- GI bleeding has a wide variety of differential diagnoses and potential workups.
- One of the fundamental determinations is **Upper** (proximal to the ligament of Treitz) versus **Lower** (distal to the Ligament of Treitz) Bleed. While no single finding on history or physical definitively determines the location, there are findings that are more suggestive of one versus the other.
- **Hematemesis** is vomiting blood.
- The blood must be near the "in hole" for it to come back out.
- **Melena** is dark tarry stools indicative of long-standing blood in the GI tract.
- **Nausea**, **Vomiting**, **Hematemesis**, and **Melena** are all indicative of an Upper GI bleed.
- Meanwhile, **diarrhea**, **FOBT ⊕**, and **Hematochezia** (bright red blood per rectum) are indicative of a **lower GI bleed.**

UPPER GI BLEED	LOWER GI BLEED
↑Ligament of Treitz Hematemesis and Melena N/V 66% of all GI Bleeding	↓Ligament of Treitz Hematochezia and Diarrhea FOBT ⊕ 33% of all GI Bleeding
CAUSES UGIB	**CAUSES LGIB**
Oropharyngeal Bleed Epistaxis Erosive Esophagitis Gastritis or Ulcer Varices Mallory-Weiss / Boerhaave Dieulafoy's Lesion Neoplasm	Diverticular Hemorrhage Angiodysplasia Colitis Anorectal / Hemorrhoids Polyps Neoplasm


GI BLEED
1) Stabilize the Patient
2 Large Bore IVs
IVF, Type and Cross,
Blood Prn. Coags/FFP
2) Determine if the bleeding is UGIB or not
EGD
⊖ for Blood
⊕ for Blood
LGIB
UGIB
Endoscopy
Varices
AVM
Boerhaave
Gastritis
Mallory Weiss
Aortoenteric Fistula
Neoplasm
Dieulafoy's
CBC ±
Transfusion Rate
<0.5cc/min
≥ q1d 1UpRBC
Slow ↓ H/H
>2cc/min
≥ q4H 1UpRBC
Rapid ↓ H/H
Slow Bleed
Brisk Bleed
Colonoscopy
Arteriogram
Locate, Diagnose, Cauterize/Embolize
⊕
⊖
Colonic Bleeding
Small Intestine
Tagged RBC
OR
Pill-Cam Endoscopy
Colitis
Neoplasms
Hemorrhoids
Diverticular Hemorrhage

Initial Management

- Determining **stability** is the 1st order of business; make the things that will keep the patient alive the priority.
- Obtaining **2 large bore IVs, Type + Cross,** and **CBC** are essential.
- **Transfusions** may be required for absolute anemia (Hgb < 7) or symptomatic anemia at any Hgb.
- **PT/PTT** determines if there's a clotting/bleeding problem or if **FFP** is required.
- Finally, **EKGs** will rule out risk for mesenteric ischemia.

Work-Up = Find the Bleed

- The simplest test one can do is to place an **NG Tube.**
- If the fluid is **green** the sample's been taken from the stomach and the duodenum and has effectively **ruled out Upper GI bleed.**
- Alternatively, if **frank blood** or **coffee grounds** were found it's highly suspicious for UGIB. Since blood tends to flow downstream an **Endoscopy** is the ***best test for UGIB***. It'll help identify lesions that are ***currently bleeding (+ propose a therapy).***

If the NG is negative do an EGD in almost all cases.

- The next step is to move to the colon.
- Here, the decision's based on if there's ***a lot of bleeding*** (Brisk Bleeding is **>2cc/hr** or **1Unit pRBC q4H**), ***slow bleeding*** (**<0.5cc/hr** or **1Unit pRBC q1day**), or ***no bleeding*** (**none**).
- The idea is since blood is moving downstream, attempting a colonoscopy with brisk bleeding will just visualize a river of blood coming at you (not very useful), while trying to find the source of a very slow bleed with an angiogram might not show anything.
- A tagged RBC study can find the source of the bleed - especially in locations where the colonoscopy can't reach - but is unable to offer any intervention.
- A pill cam is the last resort; it's notoriously unsuccessful for finding a bleed.
- In general, testing goes like this:

1) **Brisk Bleed** → **Angiogram** = Possible intervention

2) **Slow Bleed** → **Tagged RBC** = Localization only

3) **No Bleeding** → **Colonoscopy** = Definitive diagnosis

Etiologies → Management

a) Esophageal Varices

- Caused by **↑Portal HTN** secondary to liver failure, portosystemic shunts form and these veins become engorged.
- Vomiting or retching causes them to **bleed,** which is NOT self-limiting and may be fatal.
- The patient is **NG Tube ⊕, Hematemesis ⊕**, and the **EGD** shows the **definitive diagnosis.**
- In a patient bleeding right now with known variceal bleeding, give **octreotide.**
- With Endoscopy there's the option to do **cautery, banding,** or a **balloon tamponade.** Tamponade is merely a temporary bridge to a **TIPS** procedure, where the portal pressures are reduced by bypassing the cirrhotic liver (which also increases the risk of asterixis and hyperammonemia).
- Finally, **Propranolol low dose** (10mg tiD) may actually shrink varices and decrease the risk of bleeding.

b) Mallory-Weiss Tear

- Present in people who go on a drinking binge or are **one-time vomiters** who produce **hematemesis after retching.**

- The bleeding is usually **self-limiting**; it's caused by a tear in the **mucosa only** at the GE Junction.
- Perform an EGD if the patient presents with active bleeding.

c) Boerhaave Syndrome

- Present in **Alcoholics** or **Bulimics** who present like a sick Mallory-Weiss.
- They have a **transmural** tear that isn't self-limiting. They'll have **Hematemesis, Fever, Leukocytosis** and **Esophageal Crepitus.**
- The **Hamman's Crunch** is a crepitus heard with each heartbeat, indicating there's air in the mediastinum.
- These patients require emergent surgical intervention.
- Diagnose them with a **gastrografin swallow** (water soluble but less harsh than barium on the mediastinum) and follow up with an EGD.

d) Dieulafoy's Lesion

- An **anatomic variant** in the cardia of the stomach, this lesion is a superficial artery that becomes easily eroded by gastritis or ulcers.
- It presents as **sudden massive UGIB** and often requires subtotal gastrectomies.

e) Esophagitis

- Just a simple inflamed **esophagus** can bleed - especially as the **inflammation** progresses to cancer.
- Think of **GERD 1st**, but also consider **CMV** or **Herpes** (ganciclovir or foscarnet), **Candida** (nystatin), and **HIV** (HAART).
- Biopsy and culture on EGD yield diagnosis..

f) Gastritis/Ulcers

- NSAIDs (multiple shallow ulcers), Malignant (heaped up margins, necrotic core), or Acid-Induced ulcers may erode into blood vessels or perforate.
- Diagnose with EGD and treat with PPIs or resection.

g) Colitis

- Ulcerative Colitis, in particular, may present as a **bloody diarrhea** diagnosed by EGD with biopsy.
- Control the flares with steroids and control the bleeding.
- Other forms of colitis, including **bacterial infections,** should be excluded with **Stool Culture** and treated with **antibiotics.**

h) Diverticular Hemorrhage

- While ***diverticuli*** occur more often on the **left than the right,** ***hemorrhage*** occurs on the **right more than the left.** An arteriole in the dome of the diverticulum tears, which produces massive **LGIB** and **hematochezia.**
- Resection or cautery will cure the lesion.

i) Cancer

- Cancer can cause an UGIB if in the stomach or esophagus, or a LGIB if in the colon.
- Cancer has its own specific screening, diagnosis, and treatment based on which cancer it is.
- Regardless, the general principle of a camera (**endoscopy with biopsy** or **colonoscopy with biopsy**) is required for diagnosis.
- **Stage** with (PET)CT and treat with **resection** or **chemo/radiation.**

j) Mesenteric Ischemia

- This is the ***gut's equivalent*** of a "heart attack."
- Caused by **atherosclerosis** or **A fib,** the mesentery dies.
- This hurts.
- Chronic mesenteric ischemia will present with **postprandial abdominal** pain (intestinal angina) and likely weight loss.
- Acute mesenteric ischemia presents with **pain out of proportion** to the physical exam.

- An angiogram is diagnostic and resection is usually necessary.

k) Ischemic Colitis

- Ischemic colitis occurs at the watershed areas of the colon during periods of hypotension.
- This is often painful, results in a self-limiting bleed, and needs a **colonoscopy** to definitively diagnose.
- There are many other causes of GI Bleed.
- It becomes paramount to focus on the classic presentations of some of the more common and identifiable diseases, but most importantly, on **stabilizing** the patient before worrying about which diagnosis it truly is.

IBD

Ulcerative Colitis

- UC is an **inflammatory disease** is a **superficial inflammation** that's **limited to the colon**.
- Patients present with **bowel urgency, frequent bowel movements**, and **bloody diarrhea**.
- Onset is abrupt and patients often remember when the disease first started.
- Abdominal pain is unusual; it represents a complication.
- Diagnosis revolves around **colonoscopy**.
- UC is a **continuous** lesion, involving the rectum and then extending variably through the colon.
- UC doesn't extend outside the colon. The end of involved tissue is also **abrupt**.
- Biopsy of the colon reveals **crypt abscesses** and **superficial inflammation**.
- ***Extra-intestinal manifestations*** include **primary sclerosing cholangitis** (association with **p-ANCA**), erythema nodosum, and aphthous ulcers.
- Unlike with Crohn's, **surgical removal of UC is curative**. Because there's a high association with malignant transformation of UC, a **colonoscopy screening** begins at **8 years from diagnosis** and continues **annually** until resection.
- Disease severity dictates medical management.
- ***For mild disease***, **5-ASA compounds** are effective in UC (unlike Crohn's).
- ***For moderate disease***, immune modulators such as **Azathioprine** and **6-mercaptopurine** are used; **TNF-inhibitors** are used should they fail.
- Surgery is ultimately curative.

UC Flare

- Flares will present with increased number of bowel movements or worsening blood.
- For flares, **infectious etiologies must be ruled out**, specifically C. Diff.
- Flares are treated with **steroids** and **antibiotics**.

Mild: **5-ASA Compounds** designed to prevent flare by releasing in the rectum to quiet inflammation. These work for UC

Sulfasalazine

Mesalamine

Mod: **Oral steroid** taper quells the acute flare Then: follow with **immune modulators**

Prednisone

Azathioprine / 6-Mercaptopurine

Severe: **IV steroids** to quell acute flare, then:

For UC → **Infliximab** or **Cyclosporine**

For UC → Resection

SURGERY IS CURATIVE

Screening colonoscopy **q1y** starting at **y8**.

Crohn's Disease

- Crohn's disease is an **inflammatory disease** of the bowel **that can extend from the mouth to anus** and can be discontinuous (skip lesions).

- Patients present with an insidious onset of symptoms and rarely remember the initiation of the disease.
- They also present with gradually worsening **watery diarrhea** and **weight loss**. Because the inflammation is transmural, it's possible to develop **fistulas** from the bowel to any other organ (enteroentero, entero-vagina, entero-vesicular) or the skin (enterocutaneous). Because the inflammation can occur anywhere, symptoms are highly variable, which includes nutritional deficiencies.
- There's a predilection for the **terminal ileum** resulting in **B12 deficiency**.
- Diagnosis revolves around **endoscopy** and biopsy.
- Biopsy will reveal **transmural inflammation** and **non-caseating granulomas**.
- Extraintestinal manifestations exist, but aren't as specific as in UC.
- For Step 2, consider Crohn's as having, "no extraintestinal disease," though do know that Rheumatologic complaints can exist.
- There's no increased risk of malignancy in Crohn's*.
- **Resection** is **NOT curative**, but can be used on limited stretches of bowel that are refractory or particularly burdensome.
- 5-ASA compounds are still used in Crohn's disease, but there's increasing evidence that **early initiation of disease modifying** agents is superior for the disease course.
- Azathioprine and 6-mercaptopurine are used in mild and moderate disease.
- **Anti-TNF** medications are used in severe disease, and, in the absence of infection, are often successful in healing enterocutaneous fistulas.
- **Dexa-scans** and **Calcium repletion** are usually needed.

Crohn's Flare

- Flares will present with increased number of bowel movements, weight loss, and **electrolyte abnormalities**.
- For flares, **infectious etiologies must be ruled out** - specifically C. diff.
- Flares are treated with **steroids** and **antibiotics**.

Perirectal disease, such as perianal **abscess**, must be **drained**.

Mild: **5-ASA Compounds** don't really work for Crohn's disease.

Sulfasalazine

Mod: **Oral steroid** taper quells the acute flare
Then: follow with **immune modulators**

Prednisone

Azathioprine / 6-Mercaptopurine

Severe: **IV steroids** to quell acute flare, then...

For CD → Infliximab

DO NOT PERFORM SURGERY except for

Fistulas

Antibiotics are good when there's a perirectal abscess, otherwise no benefit

*severe distal colonic Crohn's = Screen like UC.

JAUNDICE

Introduction and Differential

- Jaundice is a clinical finding where there's **yellowing** of the sublingual region (1st), the **sclera** (2nd) and then the **skin** (3rd).
- It's a result of elevated **bilirubin** in the blood.
- Bilirubin is processed by the liver and excreted into the small intestine by the biliary tree.
- Defects in any three regions can cause a build up of bilirubin: 1) **PreHepatic,** which essentially means **hemolysis** producing an unconjugated bilirubinemia from increased RBC turnover, 2) **Intrahepatic**, a defect in anything involving **uptake, metabolism**, or **excretion** of bilirubin producing an unconjugated bilirubin, and 3) **PostHepatic**, typically a **mechanical obstruction** preventing efflux of conjugated bilirubin.

onjugated vs Unconjugated

- ***Unconjugated bilirubin*** comes from broken down red blood cells.
- ***Glucuronyl Transferase*** is an enzyme in the liver that **conjugates** the unconjugated bilirubin. Conjugated bilirubin can then be excreted in the GI tract.
- **Unconjugated** is generally the "worse" type. It **can't be renally excreted** and **can cross the blood brain barrier** because it's lipid-soluble.
- **Conjugated** on the other hand is water-soluble and **is renally excreted,** but **can't cross the blood brain barrier**. A conjugated hyperbilirubinemia will therefore present with **dark urine**.

Hemolysis

- Look for a **history of transfusions**, culpable medications (like **Dapsone**), or **African Americans**.
- Since actual hemolytic anemia rarely causes jaundice, look only for a mild elevation of the bilirubin.
- A **blood smear** and **Hgb Electrophoresis** can distinguish hemolytic subtypes.

2) Gilbert's and Crigler-Najjar

- Disease of uptake of bilirubin. They're either **fatal early** (Crigler-Najjar) or present as **asymptomatic jaundice** when the body is **stressed** (infection, dehydration, etc). Because bilirubin can't enter the liver or get conjugated, there's an ↑ **unconjugated bilirubin**.

3) Dubin-Johnson and Rotor syndrome

- Diseases of excretion of already conjugated bilirubin, these cause an **asymptomatic jaundice** when the body is **stressed** just like Gilbert's. However, there's **conjugated hyperbilirubinemia** so the urine will be **dark** and **for blood** (representing the bilirubin, not actually hematuria). Being able to separate these two diseases isn't necessary.

4) Gallstones

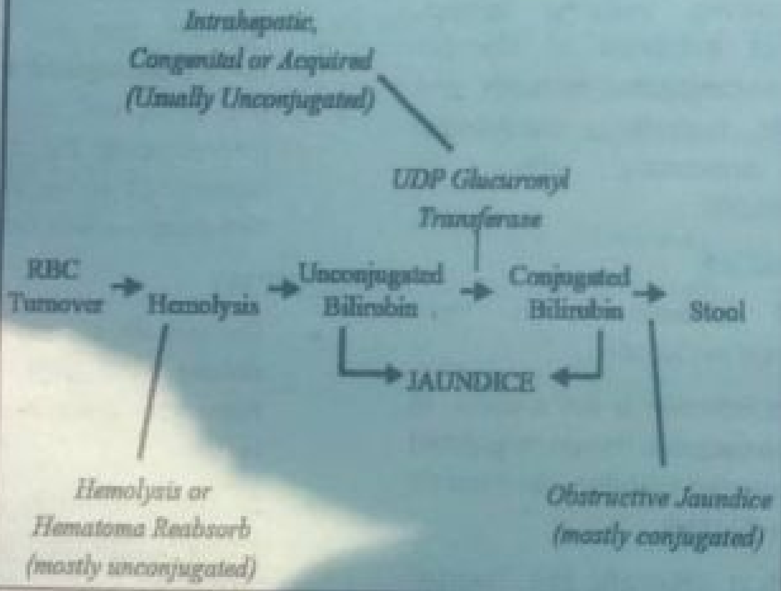
- The patient will present with a history of **colicky RUQ pain** and will have either **hemolytic anemia** or be **fat, fertile, + forty**.
- Diagnosis is made with **ultrasound** then treated/confirmed with **ERCP** to remove stones.
- Gallbladder jaundice is painful obstructive jaundice.

5) Pancreatic / Biliary Tract Cancer

- There will be a painless **obstructive jaundice** with a conjugated hyperbilirubinemia.
- An **ultrasound** will show a **thin-walled, distended gallbladder**.

Prehaptic	Hemolysis Hematoma
IntraHepatic	Gilbert's Crigler-Najjar Dubin-Johnson Rotor's Cirrhosis
PostHepatic	Gallstones Pancreatic Cancer PBC PSC

UNCONJUGATED	*CONJUGATED*
Lipid-Soluble	Water-Soluble
Crosses BBB	Ø Cross BBB
Ø Urinary Excreted	⊕ Urinary Excretion
⊕ Kernicterus	Ø Kernicterus


Intrahepatic,
Congenital or Acquired
(Usually Unconjugated)
UDP Glucuronyl
Transferase
RBC
Turnover
Hemolysis
Unconjugated
Bilirubin
Conjugated
Bilirubin
Stool
JAUNDICE
Hemolysis or
Hematoma Reabsorb
(mostly unconjugated)
Obstructive Jaundice
(mostly conjugated)

6) Primary Biliary Cirrhosis

- **PBC** is for **Bitches**, an **autoimmune disease** affecting **females** and **intrahepatic ducts**.
- Conjugated bilirubin can't get out, causing a **conjugated hyperbilirubinemia**.
- The only diagnostic tool is a **biopsy** and treatment is **transplant**.

7) Primary Sclerosing Cholangitis

- An **autoimmune** disease affecting **MALES** with an association with **ulcerative colitis** (p-ANCA). This affects **extrahepatic duc** causing a macroscopic pattern of disea
- A diagnostic **MRCP** can be used to se **beads-on-a-string** pattern.
- Biopsy (not needed) via ERCP will sho **onion-skin fibrosis**.

8) Stricture

- Stricture is the **other painless obstruct jaundice**.

- It presents just like a cancer (insidious, dilated ducts, conjugated hyperbilirubinemia), but there isn't cancer or PSC.
- Strictures are diagnosed with MRCP, confirmed by ERCP and treated with stenting (do not stent PSC, only stents).
- To identify a potential stricture look for iatrogenic causes - especially a history of manipulation of the biliary tree surgically or with ERCP.

Disease	Bilirubin	Dysfunction	Patient Picture	Diagnosis	Treatment
Hemolysis or Hematoma	Unconjugated	PreHepatic	African American, Transfusions, Medications	Heme/Onc Lectures	
Cirrhosis (any acquired form)	Unconjugated	IntraHepatic	EtOH, Viral, Wilson's, Hemochromatosis, Acetaminophen toxicity, etc. etic.	Diagnose underlying dz	Supportive Care
Gilbert's Crigler-Najjar	Unconjugated	IntraHepatic	Asx, Unconjugated Hyperbili, Death in Infancy	Genetics Biopsy	Asx, ØTx
Dubin-Johnson Rotor	Conjugated	IntraHepatic	Asx Conjugated Hyperbili	MRI, Biopsy	Asx, ØTx
Gallstones	Conjugated	PostHepatic	h/o colicky pain, RUQ worse with fatty food, Female, Fat, Forty, or Hemolysis	U/S RUQ ERCP, HIDA	ERCP
Pancreatic Cancer	Conjugated	PostHepatic	Weight Loss and Asx Jaundice	U/S RUQ CT Scan	Surgery
Primary Sclerosing Cholangitis	Conjugated	PostHepatic	MALE with Ulcerative Colitis Extrahepatic Dilation	p-ANCA MRCP Biopsy	Transplant
Primary Biliary Cirrhosis	Conjugated	PostHepatic	FEMALE with conjugated hyperbili	AMA Biopsy	Transplant
Cancer	Conjugated	PostHepatic	Weight loss, Painless Jaundice	CT scan EUS biopsy	Resection
Stricture	Conjugated	PostHepatic	Previous manipulation of the biliary system, painless jaundice	U/S RUQ MRCP	Stent

MALABSORPTION

Introduction

- Digestion begins with mastication and amylase in the mouth, continues into the stomach with gastric acid, and completes in the duodenum.
- Absorption then occurs in the "lower GI tract" south of the Ligament of Treitz.
- **Fats** require **bile salts** and a **terminal ileum** to be absorbed.
- Fat absorption has to happen for absorption of vitamins **ADEK.**
- The **proximal** bowel is the site of absorption for the **FIC** vitamins (Folate, Iron, Calcium).
- **Protein** is required for growth and needs **pancreatic enzymes** to be digested.
- Some **general malabsorption** syndromes follow.

Celiac Sprue

- This is an **autoimmune** disorder caused by a gluten **allergy**; the body produces antibodies in reaction to gluten of wheat, rye, and barley.
- Antibodies cause a destruction of intestinal villi, ↓surface area and prevent absorption of everything.
- That yields the **classic symptoms** (chronic diarrhea, weight loss, abdominal distention).
- Since the small bowel also absorbs **FIC** the **non-classic** symptoms are anemia (↓ Folate and Iron) and osteoporosis (↓ Ca).
- Diagnosis begins with anti-endomysial and **anti-transglutaminase antibodies (best).**
- Anti-gliadin antibodies aren't useful. Confirmation is made with a **biopsy** via **EGD** showing **atrophic villi**. Because it's an autoimmune disorder, withdrawal of the offending agent will show improvement - but only after antibodies diminish **(3-4 months).**
- Finally, **Dermatitis Herpetiformis** is a cutaneous variant of celiac (all DH have celiac, all celiac has DH).

Whipple Disease

- When malabsorption occurs with systemic symptoms ("malabsorption plus") think Whipple Dz. There's a **malabsorption** with **brain, lymph,** and **joint** problems.
- Caused by the organism **T. whipplei,** the bug can either be seen as PAS **Macrophages** on EGD Biopsy or via Electron Microscopy.
- Additionally, **PCR** on the **Blood/CSF** can yield a positive result.
- This requires **Long-Term Abx** to eradicate (pick either Bactrim DS or Doxycycline).

Tropical Sprue

- A distractor for celiac, it's also called sprue b/c it causes **atrophic villi** on biopsy that occurs in Caribbean farmers. It's likely due to an **infection** and thusly doesn't improve with gluten withdrawal. However, it does respond to antibiotics.

Lactase Deficiency

- As the body ages the amount of Lactase decreases.
- When lactose (i.e. **dairy products**) is consumed the sugar is not digested or absorbed; it's passed to the colon.
- Bacteria in the colon love lactase, eat it, and produce lots of gas.
- Lactose is an osmolar load that draws water into the lumen.
- This causes **foul flatulence, diarrhea,** and **bloating. Immediate improvement** can be seen by the **elimination of dairy** or adding **lactase.**
- Invasive procedures are required for diagnosis or therapy.

Pancreas/Bile Salts

- Either an obstruction (**cystic** fibrosis, **gallstones**) or destruction (chronic **pancreatitis**) causes insufficient digestive enzymes.

GASTRIC DISORDERS

Gastroparesis

- Gastroparesis ("think Gastro-paralysis") is a nerve problem with the stomach whereby digested food just won't go forward.
- In other words, the stomach can't empty.
- The **most common cause** is **idiopathic**, though it's often associated with autonomic neuropathy, especially **diabetic neuropathy** (neuropathy of the vagus nerve).
- **Chronic nausea, vomiting, and early satiety is classic for gastroparesis.**
- Severe abdominal pain isn't typical it.
- However, on inpatient medicine rotations you'll encounter patients suffering with intractable pain secondary to their gastroparesis.
- The diabetic with gastroparesis must have peripheral neuropathy in their feet for the diagnosis – the ***longest nerves are affected first.***
- Often they'll be poorly controlled as well. **Control of the blood sugar is paramount to limit diabetic gastroparesis**.
- An **endoscopy** is often performed for these patients because they present with chronic nausea and vomiting. While this can rule out other diagnoses (such as malignancy and gastric outlet obstruction), the EGD is **non-diagnostic** for gastroparesis. To diagnose it, a **gastric emptying study** is performed.
- The treatment of gastroparesis uses **prokinetic agents** as the cornerstone of therapy. **Oral Metoclopramide** is best used for chronic management while **intravenous Erythromycin** is used for acute exacerbations.
- Consuming **small meals with little fiber** also helps.
- **Avoid opiates** and **anticholinergic medications.**
- Severe, refractory cases may result in the use of gastric stimulators or tube feeds that bypass the pylorus.
- In extreme cases, parenteral nutrition may be required.

MALToma

- The "good" gastric cancer, this is a Gastric Lymphoma.
- It's caused by infection by **H. pylori**.
- It's found and diagnosed by **endoscopy with biopsy.**
- Treating the H. pylori treats the cancer. Use **triple therapy** (see peptic ulcer disease for more).

Gastric Adenocarcinoma

- One of the rarer forms of malignancy in the United States, the pathogenesis of Gastric Adenocarcinoma is poorly understood.
- **Japanese diets**, particularly those rich in **nitrate preservatives** increases the risk.
- Hence, most new gastric adenocarcinomas are diagnosed in East Asia, particularly China and Japan.
- There is currently **no screen** for Gastric Cancer. When advanced, the symptoms will be **early satiety, weight loss,** and **bowel obstruction**.
- The test of choice is **endoscopy** to diagnose, then **PET-CT** to stage.
- Most (80-90%) of adenocarcinomas are metastasized at the time of diagnosis; prognosis is poor.

ACUTE PANCREATITIS

Pathology

- Pancreatitis is caused by **autodigestion** of the pancreas by **proteolytic digestive enzymes** that are released or activated prematurely within the pancreatic parenchyma.

Etiologies

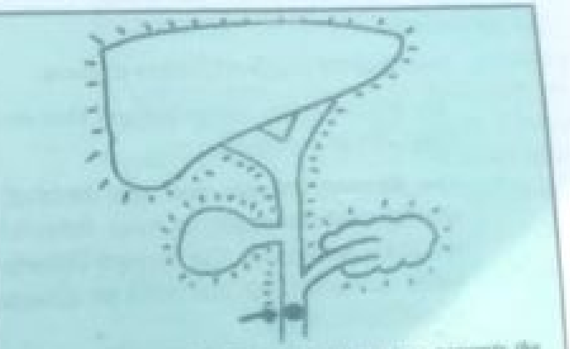
- The most common causes of pancreatitis are **gallstones** (#1) and **EtOH** (#2); they account for nearly 80% of all cases.
- For the wards, also look for iatrogenic / **trauma** (from ERCP), medications / **toxins** (HIV meds), and **hypercholesteremia**. The mnemonic "Pancreatitis" reminds you that there are many other etiologies, but they need not be assessed each time.

Parathyroid Hormone
Alcohol
Neoplasia
Calcium
Rocks (Gall Stones)
Estrogens
ACE-i
Triglycerides
Infarction (Ischemia)
Trauma (ERCP, MVA)
Infection (Mumps)
Scorpion Stings

Path	Autodigestion of the pancreas EtOH (#1) Gallstones (#2) Triglycerides
Patient	Boring epigastric pain radiating to the back, relief with leaning forward.
Dx	↑Lipase > 3x ULN ↑Amylase > 3x ULN (Lipase better) CT scan if unsure or for complications U/S if stones suspected à ERCP
Tx	NPO, IVF, Analgesia Feed when ready Antibiotics Early Refeeding ERCP only if worsening gallstone pancreatitis

Presentation

- Pancreatitis presents as a **severe epigastric abdominal pain** that will **radiate to the back**, with **relief by leaning forward** (sounds a lot like a pericarditis).
- There are also non-specific signs and symptoms such as N/V/Anorexia.
- Physical exam findings indicative of intraperitoneal hemorrhage, but associated with pancreatitis are flank ecchymosis (the **Grey-Turner Sign**) and umbilical ecchymosis (**Cullen's Sign**).



Gallstone Pancreatitis. The obstructing stone prevents the digestive enzymes from leaving the pancreas, resulting in erroneous activation and destruction of the pancreas.

Diagnosis

- This is mainly a clinical diagnosis. However, the best test is an **elevated Lipase > 3x Upper Limit of Normal** often seen in conjunction with an **Amylase**. While amylase is far less sensitive (false positives include vomiting and gallbladder disease), if either are elevated in the clinical scenario the diagnosis should be considered positive.
- A **CT scan** was once thought to be harmful, but is now known to be safe. A CT scan **isn't required** for the diagnosis, but can be used when the clinical picture is incongruent with the laboratories. Routine CT scans are not indicated.
- Other diagnostic steps are used more to identify etiologies. **Ultrasound** is done to assess for gallstones. **MRCP** is used to evaluate the biliary tree and to start work up for pancreatic cancer.

Treatment

- Initial management is **NPO Bowel Rest, IVF,** and **Analgesia**. NPO prevents pancreatic secretion. 3rd spacing can occur so IVF keeps them perfused. Analgesia keeps them from anxiety and unnecessary motion which can exacerbate the pain.
- Prophylactic Antibiotics aren't required.
- Gallstones are removed with **ERCP** only in the setting of cholangitis or when there is clinical deterioration.

Complications

- Pancreatitis is a pretty nasty disease.
- But it's the many complications that cause most of the problems.
- The ***Ranson Criteria and the APACHE II scoring systems*** exist to help determine the likely prognosis. The Ranson Criteria is easier to remember, but must be assessed at day 1 and day 3.
- The APACHE II score has more entries and is available at day 1.
- **Clinical Acumen** is as good as the scoring systems.
- DO NOT MEMORIZE these scoring systems.
- If pimped, the **BUN** has the greatest prognostic information.
- **CT scan** is the preferred method for evaluating the pancreas after pancreatitis to monitor for complications.
- Routine post-diagnosis CT scans are not indicated.

	Complication	Dx	Tx
Early	ARDS HypoCa Prognosis Pleural Effusion Ascites	CXR iCa BUN XCR U/S	Intubation Ca
Mid	SIRS Day 7	CT	Meropenem
	Infection	Bx	
Lat	Abscess	CT	Drain & Abx

- The most commonly tested complication is **pseudocyst**.
- Suspect a pseudocyst if there's early satiety or abdominal fullness 3-7 weeks after acute pancreatitis. These will **spontaneous resolve** if <6cm AND < **6weeks old**. If both are not met, then there will likely be no spontaneous resolution.
- **Surgical drainage** is required.
- Percutaneous, pancreaticogastrostomy, or open procedures can be used.
- If an infection is suspected, **don't do empiric antibiotics** unless an infection is confirmed with **biopsy**. When choosing empiric coverage, elect for **meropenem**.
- If there are **pleural effusions** or **ascites**, do **NOT** try to tap or drain them. If this fluid is a potential infectious source, then it should be drained, as should an abscess if one is identified.

Chronic Pancreatitis

- A patient that's had acute pancreatitis is at risk for developing chronic pancreatitis. It presents as **chronic pain** with occasional **acute flares**.
- The pain is identical to acute pancreatitis.
- The Lipase will be smoldering (a burned out pancreas cannot produce substantial elevations) and a **CT scan** may show **calcifications**.
- The only treatment is **pain control**, management of endocrine dysfunction (diabetes), and replacing pancreatic enzymes if necessary.
- **Surgical resection is ineffective** and should be avoided.

PEPTIC ULCER DISEASE

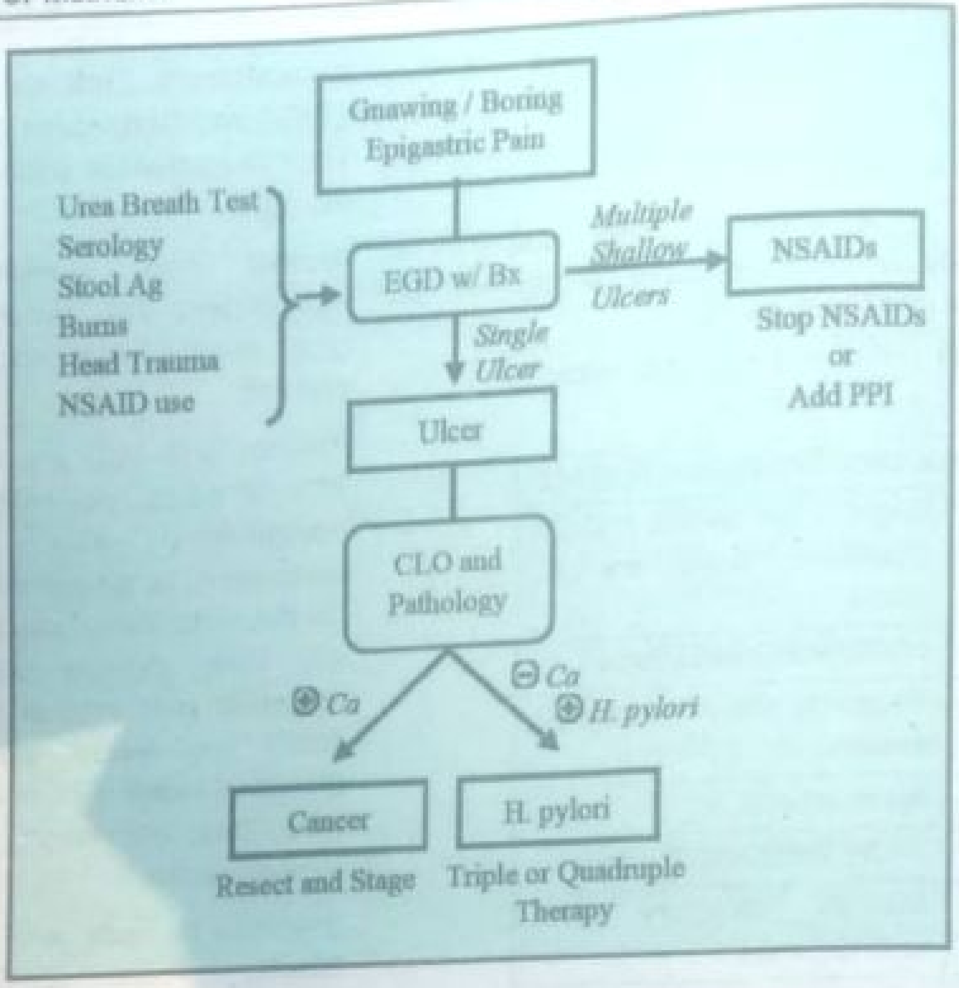
Peptic Ulcer Disease

- An **erosion** is a break < 5mm.
- An **ulcer** is a break > 5mm and histologically demonstrates going through the mucosa into the muscularis.
- **Peptic ulcer** refers to ulcers that occur in the duodenum and stomach.

Ulcer	Clinical/Endoscopic Findings
H. Pylori	Single large uncler, ~100% Duodenal ulcers are H. Pylori
NSAIDs	Multiple Shallow Ulcers
Malignancy	Necrotic base, heaped margins
Curling's	Burn patients
Cushing's	↑ ICP, Ventilated Patients
Gastrinoma	Multiple refractory ulcers with diarrhea

Ulcer	***Treatment***	***Back-Up***
H. pylori	Triple therapy	Quad Therapy
NSAIDs	PPI (STOP NSAIDs)	Sucralfate, Misoprostol, H_2 Blockers
Cancer	Resection	
Curling's	PPI	PPI PPx
Cushing	PPI	PPI PPx

- The etiology of Peptic ulcer disease can often be tracked to the appearance of the lesion on endoscopy.
- **H. pylori** and **NSAIDs** account for the vast majority (90%) of peptic ulcers.
- Others that are less common are **malignancy** and what I call the 'special circumstances: **Curling's** (Burns), **Cushing** (↑ICP) and **Gastrinoma** (Zollinger-Ellison). Their characteristic patterns are listed to the right.
- **Alcohol** and **smoking** are **NOT** independent risk factors, but worsen ulcer disease when another etiology is present.
- Patients with PUD are asymptomatic in 20% of cases, presenting only with a complication such as **bleeding**, perforation, or gastric outlet obstruction. On the tests, those who are symptomatic will likely present with a **gnawing epigastric pain** related to food. **Gastric ulcers** are **worse *with* food**, while **Duodenal ulcers** are worse **2-5 hours *after* food**. These associations are unreliable in clinical practice.
- Diagnosis is made with **Endoscopy and Biopsy**, which allows for **direct visualization to** rule out **malignancy** and definitively diagnose **H. pylori**. The diagnostic steps for H. pylori are discussed on the next page.
- Treatment revolves around acid-suppression therapy, where **Proton Pump Inhibitors** (PPIs) are superior.
- Treatment for **H. pylori** involves Triple Therapy.
- For **NSAID induced ulcers**, the NSAIDs should be discontinued at the time of diagnosis.
- If they must be restarted after ulcer **healing**, use PPI prophylaxis to prevent recurrence of ulcer.
- **PPIs are superior** to sucralfate, misoprostol, and H2 blockers for NSAID prophylaxis.


Gnawing / Boring Epigastric Pain
Urea Breath Test
Serology
Stool Ag
Burns
Head Trauma
NSAID use
EGD w/ Bx
Multiple Shallow Ulcers
NSAIDs
Stop NSAIDs or Add PPI
Single Ulcer
Ulcer
CLO and Pathology
⊕ Ca
⊖ Ca
⊕ H. pylori
Cancer
Resect and Stage
H. pylori
Triple or Quadruple Therapy

- All ulcers are helped by **Smoking Cessation, Alcohol Cessation**, and **PPIs**.
- **Repeat Endoscopy** is **NOT** needed except when the symptoms are refractory or when cancer is suspected but not diagnosed.

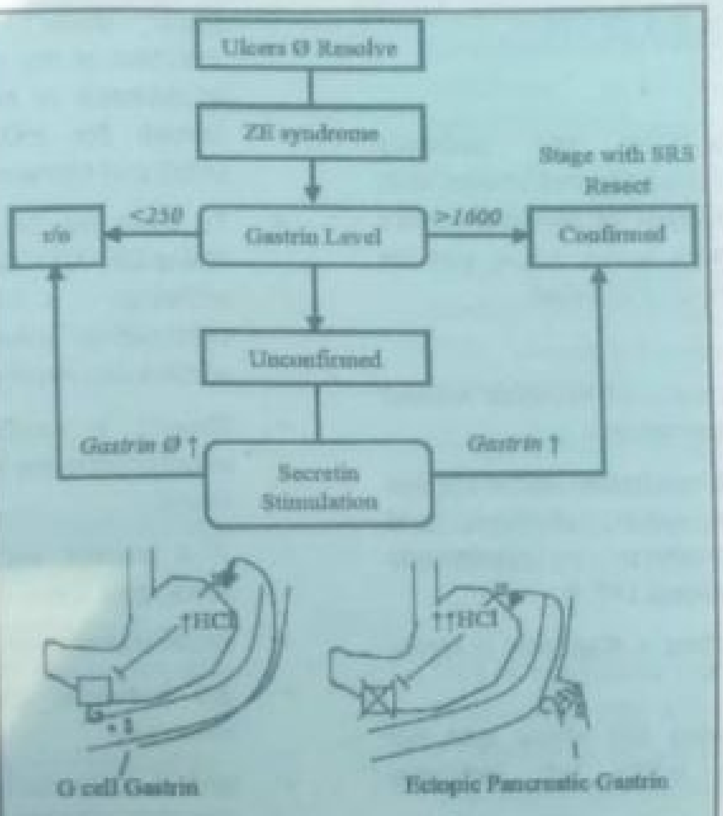
H. pylori

- Infection with H. pylori is common (about 50% of the world).
- But of those infected, only 15% will become symptomatic.
- It causes a mild pangastritis in 85% of patients, while 15% develop **ulcers**.
- A small percentage (<1%) will develop **MALToma**. Thus, **H. pylori is considered a carcinogen**.
- Testing for H. pylori is challenging. PPIs and H2 blockers **must be stopped** before doing all testing other than serology.

Test	*Use*
Serology	Treat if never treated before
Urea Breath Test	Confirm Infection
Stool Antigen	Confirm Eradication
Endoscopy	Urease Test (immediate)
Endoscopy	Histology (superior)

Triple Theropy	*Quadruple Therapy*
Amoxicillin*	Metronidazole
Clarithromycin	Tetracycline
PPI	Bismuth
	H2-Blocker

- The test and treat strategy is employed for those who haven't been treated previously and have evidence of PUD or MALToma. In a case with **symptoms** and **positive serology**, the next step is simply **to treat**.
- **Urea breath testing** is the best noninvasive test to confirm diagnosis (which means infection).


Ulcers Ø Resolve
ZE syndrome
Stage with SRS
Resect
r/o
<250
Gastrin Level
>1000
Confirmed
Unconfirmed
Gastrin Ø ↑
Gastrin ↑
Secretin Stimulation
↑HCl
↑↑HCl
G cell Gastrin
Ectopic Pancreatic Gastrin

Zollinger-Ellison. *The normal condition (left) is a balance between HCl and Gastrin production, HCl inhibiting the production of Gastrin. The ZE-condition (right) causes constant HCl production, depression of the G cells, but unopposed gastrin stimulation of acid.*

- **Stool antigen testing** is the best method to confirm eradication.
- **Endoscopy with biopsy** is the gold standard. Either the **rapid urease test** (used in real time in the endoscopy suite) or **histology** can be used to confirm the presence of the bug.
- **Triple therapy** consists of clarithromycin, amoxicillin, and a PPI; it's superior to quadruple therapy.

Zollinger-Ellison / Gastrinoma

- In the presence of **virulent** or **refractory** ulcers despite adequate therapy, consider ZE. This is especially true when considering **Ulcers** and **Diarrhea** together.
- Caused by a cancer in the head of the pancreas, this endocrine tumor **erroneously secretes Gastrin** causing ↑ production of gastric acid. ↑ Acid = ↑ Mucosal Barrier Destruction = ↑ Ulcers.
- Test for this disease by first getting a **serum gastrin level.** If the levels of gastrin are very elevated (in the 1000s) a Secretin Stimulation Test isn't required.
- If the value is < 250, the diagnosis is excluded.
- **PPIs** must be held as they can falsely increase Gastrin levels. If equivocal follow with a **secretin stimulation test** which will cause an ↑ **Gastrin**.
- Once confirmed, localize the tumor with a **Somatostatin Receptor Scintigraphy** (SRS) scan. CT scans often aren't sensitive enough.
- While the gastrinoma itself is **benign,** it must be resected to prevent future ulcers. Additionally, high levels of gastrin can transform the normal stomach mucosa into a **malignant gastric cancer.**

VIRAL HEPATITIS

Introduction

- Viral Hepatitis is an umbrella categorization of the different viruses that can cause an infection of the liver. Some are chronic, others acute, some can be prevented, others only avoided.

Hepatitis A

- This is an **Acute** form of hepatitis spread by fecal-oral contamination.
- It has a 2-6 week incubation and is carried in contaminated water, shellfish, and **daycares**. It produces a **nonbloody diarrhea** and a **modest LFT ↑**.
- Since it's self-limiting a diagnosis is rarely required.
- However, serologies will show **IgM** for active infection while **IgG** indicates immunity.
- A **vaccine** is available and given as a child.
- Boosters are recommended for travel to endemic regions >2 wks before the trip.
- **Post Exposure Prophylaxis** with IgG can be started **with vaccine** within 2 weeks of exposure.

Hepatitis B

- This can be **both** acute and chronic.
- The stronger the immune response the less likely it's in the chronic carrier state and more likely it's a devastating hepatitis case.
- **Adults** acquire it through **Sex** more than **IVDA.** Because adults are generally healthy (an intact immune system) they suffer **jaundice, LFTs in the 1000s,** and only the acute phase without chronic carrier state.
- **Fulminant Hepatitis** is rare (and nearly fatal).
- **Babies** acquire it through the **birth canal** (vertical transmission) and will likely have **symptoms** (a poor immune system), but are almost always **chronic carriers.**
- Since there's chronic inflammation infection of the chronic carrier may result in **cirrhosis** or **hepatocellular carcinoma.** **Screen for HCC** with **Alfa-fetoprotein** (AFP) and **Ultrasound**.
- To treat the hepatitis infection give **peg IFN-α-2a** for ***48 weeks*** coupled with antivirals (lamivudine, adefovir, telbivudine, entecavir) with the goal of eliminating HBeAg.
- There's a vaccine against Hep B so **vaccinations** are a must to prevent chronic illness.
- If a patient isn't vaccinated and gets stuck, give them **vaccine** and **ppx IgG**.
- Understanding serology is critical.
- **IgG** indicates either past exposure or immunity.
- **IgM** is only during acute infection. The virus has a surface antigen (HBsAg), a core antigen (HBcAg), and a protein of infectivity (HBeAg).
- **IgG HBsAb ONLY** is a sign of **vaccination**.
- **IgG HBeAb** but without the presence of Antigen is a sign of immunity following exposure.
- **HBsAg** (the presence of antigen, not antibody) occurs early and denotes infection.
- **HBeAg** indicates active infection and **infectivity**. During the **window period** where the Antibodies and Antigens cancel each other out (binding to each other prevents binding of the test antigen), Anti-HBc is the only indicator of infection. Incubation is generally **1-6 months.**

Fecal Oral

RNA

Vaccine ⊕

IgM = Active Infxn

IgG = Immunity

PPX = IgG w/I 2 weeks of exposure

IVDA/Sex = Adult = Acute

Baby = Vertical = Chronic

HCC/Cirrhosis if chronic

HBsAg initial infxn

HBeAg infectivity

IgM HBxAg window period

IgG HbeAb waning infection / infectivity

IgG HBsAb long term immunity

Vaccine ⊕

PPx = IgG

DNA Virus

Peg-If-α-2a + antivirals = ↓ HCC Transformation

Hep C

- Hep C is the **chronic** hepatitis that has **no vaccine.** Until recently there was also no treatment.
- Hepatitis C is on its way to eradication.
- Good thing too - chronic hepatitis is chronic inflammation, leading to **cirrhosis** after 20-30 years.
- Cirrhosis progresses to **hepatocellular carcinoma** at a rate of 2-5%.
- Even in the absence of cirrhosis, chronic Hep C can lead to hepatocellular carcinoma.
- Hep C is transmitted by **blood** and essentially not at all by sex (people who sleep with people who do IV drugs tend to also do IV drugs, which is how they get the virus).
- Blood transmission means **IVDA** and **Blood Transfusions.**
- The goal with all Hep C is to **prevent further inflammation** by abstaining from alcohol and to **screen for HCC** with annual Ultrasound and AFP.

Requires coinfection with Hep B makes B worse

- There are two treatments for Hep C.
- If genotype 1b, we can use **Pegylated Interferon with Ribavirin** which causes psychosis, depression, and flu-like symptoms for a year.
- If genotype 2 or 3, we have the new **Direct Acting Antivirals** which all end in –vir.
- There are many of them and more are coming (they're extremely effective, but also extremely expensive – expect to talk about them).
- Viral serology is either **acute** (Anti-HCV, ⊕ HCV RNA), **resolved** (⊕ Anti-HCV, ∅ HCV RNA), or most commonly, **chronic** (⊕ Anti-HCV and ⊕HCV RNA).

Hep D

- This is essentially **mini-B.** It requires the presence of **Hep B** (reliant on one of Hep B's proteins) and is transmitted the same way. It causes a **more severe hepatitis** and a **faster progression to cirrhosis.**

Hep E

- Pregnant ladies in third world countries contract it through fecaloral route. Think of this as Hep A of women in the 3rd world.

Pregnant ladies in third world countries

IVDA//Blood Transfusions = Chronic

HCC/Cirrhosis

Antibody ⊕ and HCV RNA ⊕ = Early Infection

Antibody ⊕ and HCV RNA ⊕ = Resolution (rare)

Antibody ⊕ and HCV RNA ⊕ = Chronic

NO Vaccine

PPx = IgG

RNA Virus

Peg-IF-α-2a + Ribivarin = Remission and ↓ HCC

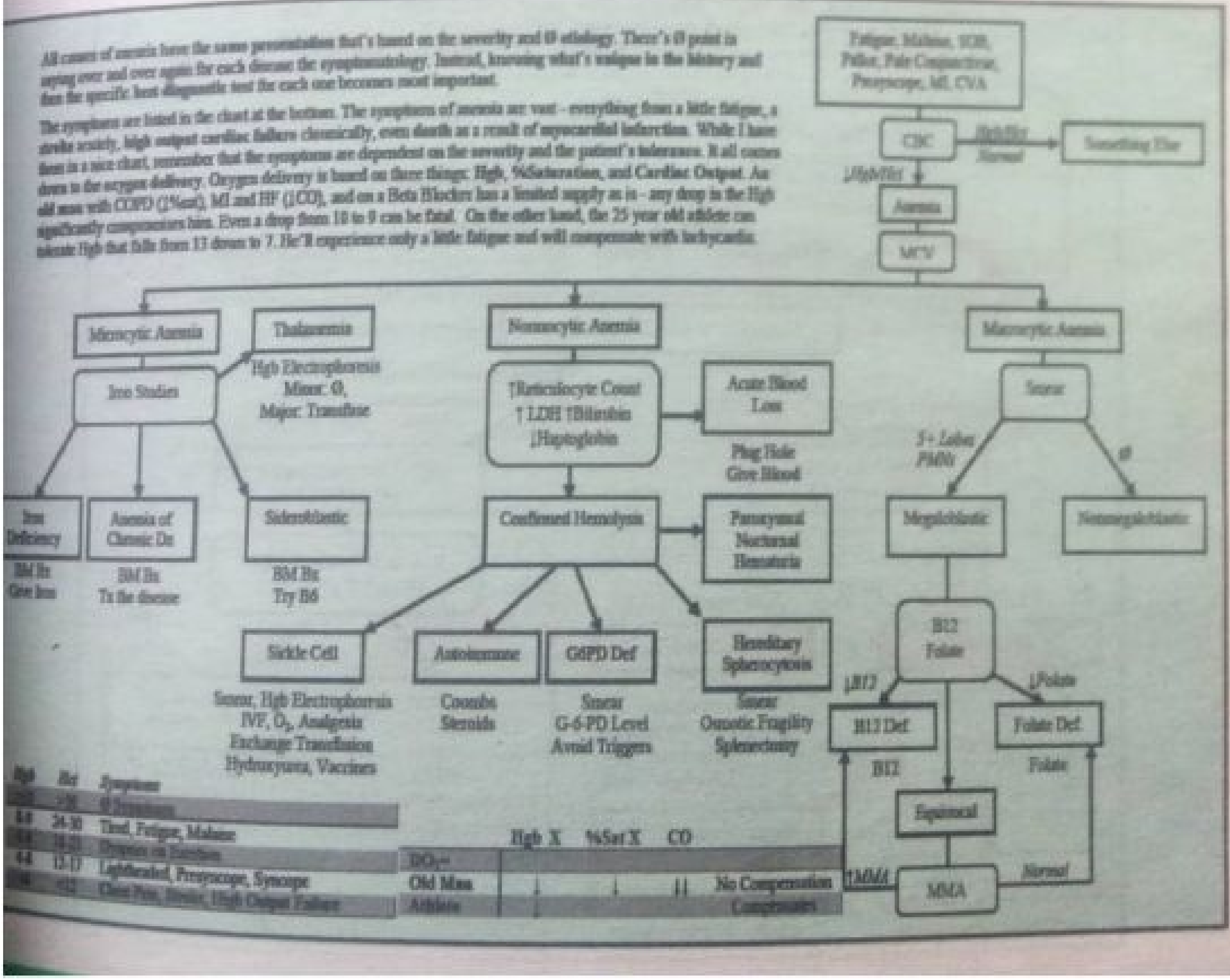
Direct Acting Antivirals = Hep C cure (~12 week regimen)

Hepatitis	*Route*	*Acute*	*Chronic*	*Cancer*	*RNA/DNA*	*Vaccine*	*Serology*
Hep A	Fecal-oral	Always	Never	Never	RNA	>2 weeks before endemic travel	N/A
Hep B	IVDA, Sex, Vertical through birthing	Strong immune = Acute	Weak Immune = Chronic	HCC, Only with chronic infxn	Incomplete DNA	All @ risk, especially health care providers	See Above
Hep C	IVDA, Horizontal, or through blood transfusions	Never	Always	HCC	RNA	None	See Above
Hep D	IVDA, Sex, requires Hep B	Never	Always	HCC	RNA	None	—
Hep E	Fecal-Oral	—	—	—	—	—	—

HEME ONCOLOGY

APPROACH TO ANEMIA

- All causes of anemia have the **same presentation** that's based on the **severity** and **etiology**.
- There's point in saying over and over again for each disease the symptomatology.
- Instead, knowing what's **unique in the history** and then the specific **best diagnostic test** for each one becomes most important.
- The symptoms of anemia are vast - everything from a little fatigue, a **stroke** ***acutely***, **high output cardiac failure** ***chronically***, even **death** as a result of **myocardial infarction**.
- Remember that the symptoms are dependent on the **severity** and the patient's **tolerance**.
- It all comes down to the **oxygen delivery**.
- Oxygen delivery is based on three things: **Hgb, %Saturation**, and **Cardiac Output**.
- An **old man** with COPD (↓%sat), MI and HF (↓CO), and on a Beta Blocker has a limited supply as is - any drop in the Hgb significantly compromises him. Even a drop from 10 to 9 can be fatal. On the other hand, the 25 year old athlete can tolerate Hgb that falls from 13 down to 7. He'll experience only a little fatigue and will compensate with tachycardia.



All causes of anemia have the same presentation that's based on the severity and Ø etiology. There's Ø point in saying over and over again for each disease the symptomatology. Instead, knowing what's unique in the history and then the specific best diagnostic test for each one becomes most important.

The symptoms are listed in the chart at the bottom. The symptoms of anemia are vast - everything from a little fatigue, a stroke acutely, high output cardiac failure chronically, even death as a result of myocardial infarction. While I have them in a nice chart, remember that the symptoms are dependent on the severity and the patient's tolerance. It all comes down to the oxygen delivery. Oxygen delivery is based on three things: Hgb, %Saturation, and Cardiac Output. An old man with COPD (↓%sat), MI and HF (↓CO), and on a Beta Blocker has a limited supply as is - any drop in the Hgb significantly compromises him. Even a drop from 10 to 9 can be fatal. On the other hand, the 25 year old athlete can tolerate Hgb that falls from 13 down to 7. He'll experience only a little fatigue and will compensate with tachycardia.

Hgb	Hct	Symptoms
[illegible]	>30	Ø Symptoms
[illegible]	24-30	Tired, Fatigue, Malaise
[illegible]	18-23	Dyspnea on Exertion
4-6	12-17	Lightheaded, Presyncope, Syncope
[illegible]	<12	Chest Pain, Stroke, High Output Failure

	Hgb X	%Sat X	CO	
DO_2=				
Old Man	↓	↓	↓↓	No Compensation
Athlete	↓			Compensates

Fatigue, Malaise, SOB, Pallor, Pale Conjunctivae, Presyncope, MI, CVA
CBC
Hgb/Hct Normal
Something Else
↓Hgb/Hct
Anemia
MCV
Microcytic Anemia
Thalassemia
Hgb Electrophoresis
Minor: Ø,
Major: Transfuse
Iron Studies
Iron Deficiency
BM Bx
Give Iron
Anemia of Chronic Dz
BM Bx
Tx the disease
Sideroblastic
BM Bx
Try B6
Normocytic Anemia
↑Reticulocyte Count
↑LDH ↑Bilirubin
↓Haptoglobin
Acute Blood Loss
Plug Hole
Give Blood
Confirmed Hemolysis
Paroxysmal Nocturnal Hematuria
Sickle Cell
Smear, Hgb Electrophoresis
IVF, O2, Analgesia
Exchange Transfusion
Hydroxyurea, Vaccines
Autoimmune
Coombs
Steroids
G6PD Def
Smear
G-6-PD Level
Avoid Triggers
Hereditary Spherocytosis
Smear
Osmotic Fragility
Splenectomy
Macrocytic Anemia
Smear
5+ Lobe PMNs
Ø
Megaloblastic
Nonmegaloblastic
B12
Folate
↓B12
↓Folate
B12 Def
B12
Folate Def
Folate
Equivocal
MMA
↑MMA
Normal

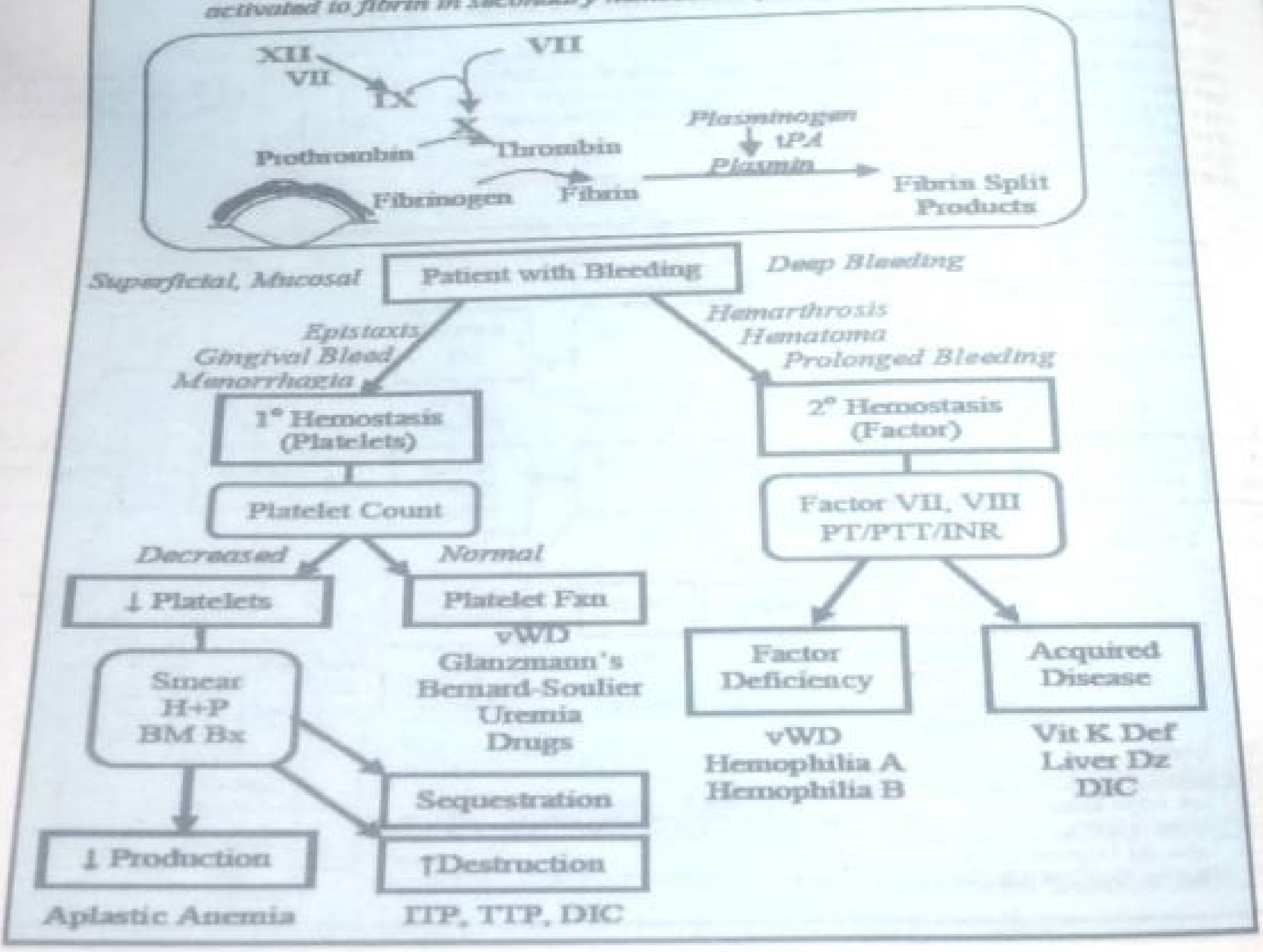
Scanned with CamScanner

BLEEDING

Introduction

- Understanding bleeding can be complex.
- Memorized the entire clotting cascade and PT/PTT valves for every disease.
- **Primary Hemostasis** is a function of **platelets** that starts with **endothelial injury**.
- From the endothelium, **von Willebrand factor** (**vWF**) is released like sticky Velcro tentacles, snatching onto platelets via **Glyc-Ib** via a process called **adhesion**.
- Adhesion activates platelets (release o granules and rearrangement of pro surface).
- This allows **fibrinogen** to link platelets vi **glycoprotein IIb/IIIa** through a proce called **aggregation**.
- The end product is a **platelet plug** tha stops the bleeding initially, with a **fibrinogen mesh** ready to start the heavy duty clotting.

Primary hemostasis begins with endothelial injury, releasing von Willebrand factor (1), sticking to platelets via Glyc-Ib, adhesion (2). This activates the platelets and allow for aggregation through fibrinogen and Glyc-IIb/IIIa. The end result is a fibrinogen mesh plug of platelets, ripe to be activated to fibrin in secondary hemostasis (shown below).


XII
VII
VII
IX
X
Prothrombin
Thrombin
Plasminogen
tPA
Plasmin
Fibrinogen
Fibrin
Fibrin Split Products
Superficial, Mucosal
Patient with Bleeding
Deep Bleeding
Epistaxis
Gingival Bleed
Menorrhagia
Hemarthrosis
Hematoma
Prolonged Bleeding
1° Hemostasis (Platelets)
2° Hemostasis (Factor)
Platelet Count
Factor VII, VIII PT/PTT/INR
Decreased
Normal
↓ Platelets
Platelet Fxn
vWD
Glanzmann's
Bernard-Soulier
Uremia
Drugs
Factor Deficiency
Acquired Disease
vWD
Hemophilia A
Hemophilia B
Vit K Def
Liver Dz
DIC
Smear
H+P
BM Bx
Sequestration
↑Destruction
↓ Production
Aplastic Anemia
ITP, TTP, DIC

- **Secondary Hemostasis** ends with fibrinogen mesh turning into **fibrin**.
- Along the way multiple clotting factors need to be activated.
- **Factor 7** is by its lonesome in the **extrinsic pathway** (measured by **PT**).
- Factors **8-12** (except 10) are in the **intrinsic pathway** (measured by **PTT**).
- The two pathways converge with the activation of **Factor 10**, which together with **Factor 5**, turns prothrombin to thrombin.
- Thrombin activates the fibrinogen mesh on those platelets to activate clotting.
- The whole deal ends by the activation of **tPA**, which dissolves the clot into **split products**.

Differential

- People like to jump to **coagulation studies** with bleeding. For the most part that's ok. Have a bleed? Get a **CBC** and **Coags**. But if interested in determining the best test for the patient in front of you, ask if they have **platelet bleeding** (superficial bleeding secondary to platelet dysfunction) or **factor bleeding** (deep bleeding secondary to hemostasis dysfunction). Then, if it's a problem with platelets use **platelet count** and **platelet function** (only if count is normal as a ↓count or ↓function) to get near a diagnosis. If it's factor bleeding use **PT**, PTT, INR, + **Factor Levels** to narrow the differential. From there each disease has its own detail, confirmatory test, and treatment.

Test	*Measuring What?*	*Diagnosis / Diseases*
PT	Extrinsic Pathway	Warfarin, Vit K, Factor 7
PTT	Intrinsic Pathway	Heparin, Lupus Anticoagulant
Bleeding Time (Platelet Fxn)	Formation of Plug	Platelet Disorder Thrombocytopenia
Factor Levels	Direct Measure	Factor Deficiency
Mixing Study	Difference Between Inhibitors	Factor Deficiency
vWF	Direct Measure	vWD
D-Dimer Fibrinogen Fibrin Split	Indirect Measure of Fibrinolysis	DIC

1. Von Willebrand Disease

- A person with a **platelet type bleeding** and a **normal platelet count** likely has vWD. If there's ↓vWF, platelets can't adhere. Adhesion = Aggregation = Plug. Start by testing for dysfunction of platelets with a **bleeding time** (archaic) or the newer **platelet function test** then get a **vWF assay**. Since vWF stabilizes Factor VIII there might also be **factor type bleeding**.
- Treat with **desmopressin** to ↑vWF. If severe, give **cryoprecipitate** or **Factor VIII** acutely.

Von Willebrand...But What About?

Glanzmann's Thrombasthenia	Deficiency of GlycIIb/IIIa
Bernard-Soulier	Deficiency of Glyc-Ib
Uremia	Seen in Renal Failure
Drugs	We give patients medications to limit clotting **ASA, Clopidogrel, NSAIDs, Abciximab**

2. Thrombocytopenia

- Get the general idea of each potential cause and learn what to look for.
- If **all cell lines are decreased** then it's an **aplastic anemia** (a production problem).
- If the **spleen is really big** it's **sequestration** (a sequestration problem).
- The other forms of thrombocytopenia all involve **destruction** of platelets.
- **Heparin-Induced Thrombocytopenia** (HIT) occurs in patients on **Heparin** (usually on day 5-7 of tx).
- To alleviate **stop the heparin** and get **HIT-Antibodies**. If the patient has the classic **pentad (↓platelets, fever, altered mental status, renal failure, Microangiopathic hemolytic anemia)** then they have TTP.
- Do a **plasma exchange** and absolutely ***avoid platelet transfusion***.
- *Finally, if* ***she*** *has a thrombocytopenia and* ***all the others have been ruled out*** *assume she has* ***ITP*** *- an autoimmune "hemolysis" of platelets.*
- *Fight with* **IVIg** or **Rhogam** right now, **steroids** chronically, and **splenectomy** if *refractory*.

Thrombocytopenia

TTP	↓ **Platelets + Fever +** **AMS + RF + MAHA**	↓Plt + ↓RBC	**Exchange** **Transfusion**	**Never give** **Platelets**
HIT	On **Heparin** 5-7d hx 3-4 d with h/o HIT	↓Plt **Only**	Stop Heparin	**Tirofiban**
DIC	DIC Any systemic or severe dz, s/p OB, s/p trauma oozing from every hole	↓Plt ↑PT ↑PTT	Tx Underlying Disease	**Plts** **cryo** **who** [illegible]
ITP	**Female** with **↓platelets** but nothing else	**↓Plt**	Plt<20 or bleeding Plt >20 **Steroids** Refractory: **Splenectomy**	IVIG

3. Hemophilia

- An X-linked recessive (**boys only**) disorder that affects **Factor 8** (type **A**) or Factor 9 (type B).
- It's a deep factor type bleeding in children (hemarthrosis is classic).
- vWD should be ruled out.
- Since Factor VIII doesn't last very long **transfuse** only when the patient's actively **bleeding**.

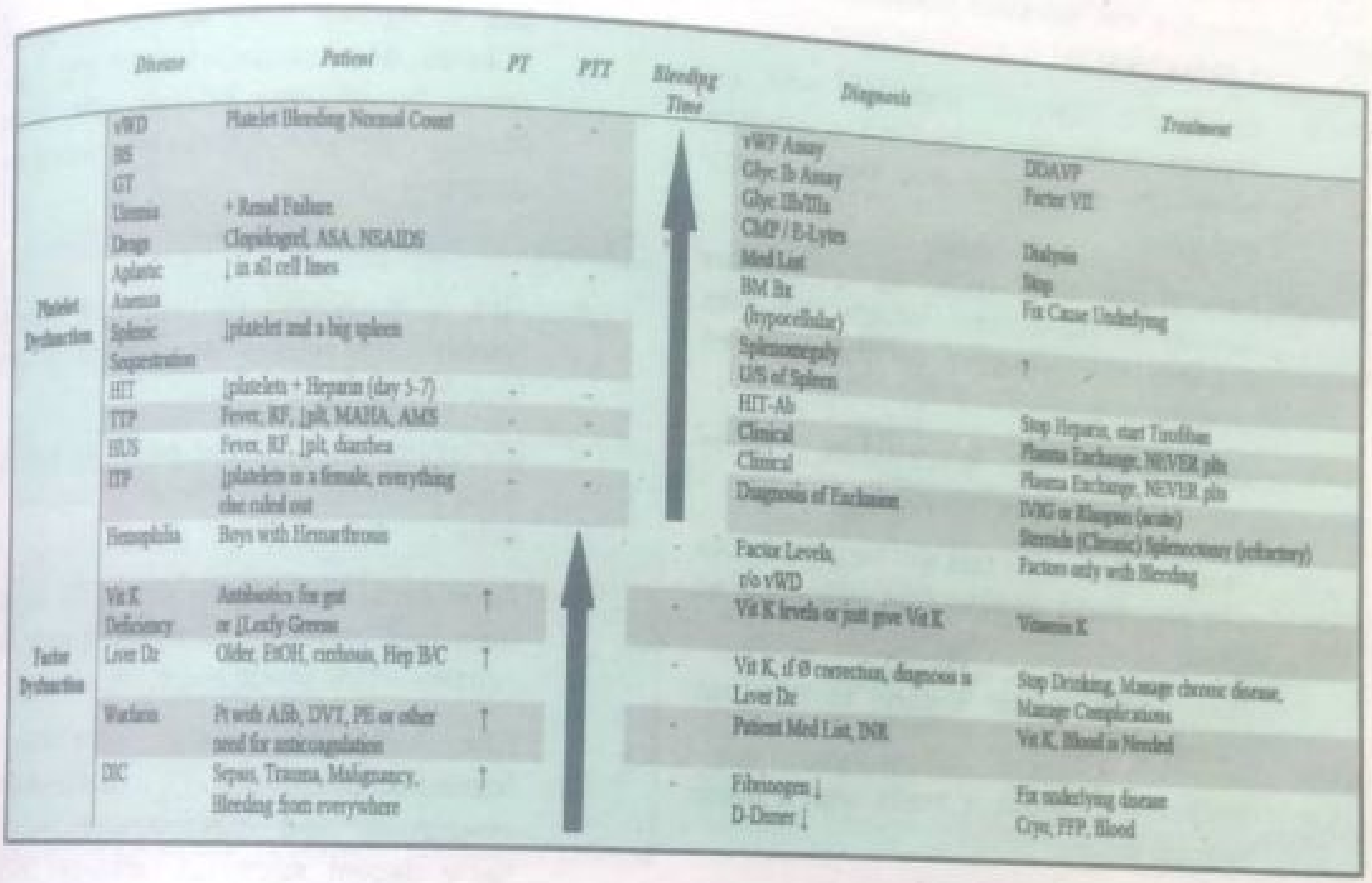
4. Liver Disease + Vitamin K Deficiency

- The liver needs vitamin K and Vitamin K needs a liver.
- Either way, factors **2**, **7**, **9**, and **10** (also protein **C+S**) are broken, messing up both the **intrinsic** and **extrinsic** pathways and producing a factor type bleeding.
- If the patient's **cirrhotic**, antibiotics killed intestinal **K-producing bacteria**, or iatrogenically we blocked the effect with **warfarin** there could be a bleed.
- The move should be to test for factor levels.
- Ultimately, however, **K will have to be given**. If there's no improvement after K it's **liver disease**.

- If it improves they were just lacking vitamin K.

3. Disseminated Intravascular Coagulation (DIC)

- Occurs in significant systemic disease (**sepsis, shock, malignancy**) where clotting goes crazy; many clots form where there should be none.
- This leaves **platelets** and **clotting factors** for where the holes actually are.
- This person bleeds from everywhere. There isn't one single test, but together an **↑ PT ↑ PTT** (factors), **↓ Fibrinogen** (except in early disease), a **+ D-Dimer / Fibrin Split Products** and the clinical history give a strong argument.
- Treat by giving everything back (**platelets, cryoprecipitate, blood**) and **fix the underlying disease**.



	Disease	Patient	PT	PTT	Bleeding Time	Diagnosis	Treatment
Platelet Dysfunction	vWD	Platelet Bleeding Normal Count	-	-	↑	vWF Assay	DDAVP
	BS				↑	Glyc Ib Assay	Factor VII
	GT				↑	Glyc IIb/IIIa	
	Uremia	+ Renal Failure			↑	CMP / E-Lytes	Dialysis
	Drugs	Clopidogrel, ASA, NSAIDS			↑	Med List	Stop
	Aplastic Anemia	↓ in all cell lines	-	-	↑	BM Bx (hypocellular)	Fix Cause Underlying
	Splenic Sequestration	↓platelet and a big spleen			↑	Splenomegaly U/S of Spleen	?
	HIT	↓platelets + Heparin (day 5-7)	-	-	↑	HIT-Ab	Stop Heparin, start Tirofiban
	TTP	Fever, RF, ↓plt, MAHA, AMS	-	-	↑	Clinical	Plasma Exchange, NEVER plts
	HUS	Fever, RF, ↓plt, diarrhea	-	-	↑	Clinical	Plasma Exchange, NEVER plts
	ITP	↓platelets in a female, everything else ruled out	-	-	↑	Diagnosis of Exclusion	IVIG or Rhogam (acute) Steroids (Chronic) Splenectomy (refractory)
Factor Dysfunction	Hemophilia	Boys with Hemarthrosis	-	↑	-	Factor Levels, r/o vWD	Factors only with Bleeding
	Vit K Deficiency	Antibiotics for gut or ↓Leafy Greens	↑	↑	-	Vit K levels or just give Vit K	Vitamin K
	Liver Dz	Older, EtOH, cirrhosis, Hep B/C	↑	↑	-	Vit K, if Ø correction, diagnosis is Liver Dz	Stop Drinking, Manage chronic disease, Manage Complications
	Warfarin	Pt with AFib, DVT, PE or other need for anticoagulation	↑	↑	-	Patient Med List, INR	Vit K, Blood is Needed
	DIC	Sepsis, Trauma, Malignancy, Bleeding from everywhere	↑	↑	-	Fibrinogen ↓ D-Dimer ↓	Fix underlying disease Cryo, FFP, Blood

LEUKEMIA

Introduction

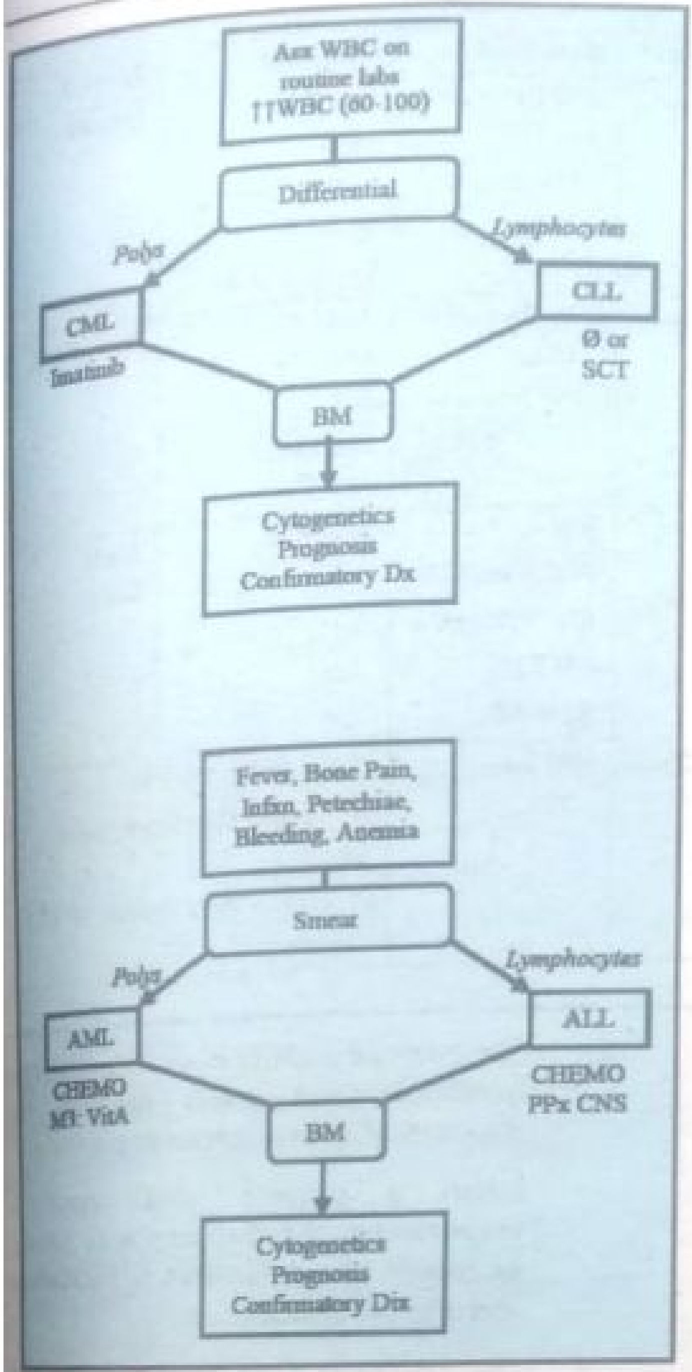
- In dealing with Leukemias we must consider whether they're **acute** (undifferentiated, aggressive) or **chronic** (differentiated, indolent).
- The **acute** leukemia patients are going to be SICK (**fever, night sweats, bleeding, and infection**).
- It's a product of useless, immature cells crowding out effective cell lines, creating a **pancytopenia**.
- Conversely, **Chronic** leukemia will be **asymptomatic** and found on a routine screen for something else (unless very late stage).
- Patients present with an **enormous** number of **leukocytes**. Which line gets elevated is dependent on the type of cancer.
- **Myelogenous** is **Neutrophils**, while **Lymphocytic** is **Lymphocytes**.
- In all cases the first test will be a **smear** to rule out acute disease (the presence of blasts).
- Then, a **differential** is done to rule out chronic disease.
- Definitive diagnosis is made with a **bone marrow biopsy**.

1. Acute Myelogenous Leukemia

- This is a disease of **immature** (acute) **neutrophils** (myelogenous) **cancer in the blood** (leukemia).
- It can arise de novo after exposure to **radiation**, **benzene**, or **chemo**, or be a transformation (so-called **"blast crisis"**) from other marrow cancers (CML, MDS).
- The symptoms of **bleeding**, **bruising**, **petechiae**, **pallor** and **fever** set in rapidly.
- CBC is of no use as all values could be ↑ or ↓.
- What gives the diagnosis away is seeing **blasts** on a **peripheral smear**.
- To confirm the diagnosis a **Bone Marrow Biopsy** showing **>20% Blasts** is required as well as **cytogenetic analysis** showing neutrophils (myeloperoxidase).
- A special form of AML, the **M3 type** (**Promyelocytic**), is diagnosed by the presence of **Auer Rods**.
- Treatment with chemotherapy (**idarubicin** + **Ara-C**) can push AML into remission.
- **M3** is treated with **Vitamin A**, which induces development out of the blast phase by **all-trans retinoic acid**. >20% blasts on peripheral blood also makes the diagnosis.

2. Acute Lymphoid Leukemia

- This is a disease of **immature** (acute) **lymphocytes** (lymphoid) **cancer** in the **blood** (Leukemia).
- It's often found in the **pediatric** patient who presents with **bleeding** and bone **pain**.
- As in AML, look at the **smear** for blasts then get a **Bone Marrow Biopsy** to confirm **>20% blasts** and cytogenics.
- Like AML, it's treated with chemo (**cyclophosphamide, doxorubicin, vincristine, and methotrexate**) with a fairly decent sustained remission (90%) and poor cure rate (50%).
- Consider doing **intrathecal ppx chemo-radiation** with **Ara-C** or **Methotrexate**, because the CNS is a sheltered region for ALL to hide while undergoing therapy for systemic blood and marrow cancer. >20% blasts on peripheral blood also makes the diagnosis.


Asx WBC on routine labs ↑↑WBC (60-100)
Differential
Polys
Lymphocytes
CML
Imatinib
CLL
Ø or SCT
BM
Cytogenetics Prognosis Confirmatory Dx
Fever, Bone Pain, Infxn, Petechiae, Bleeding, Anemia
Smear
Polys
Lymphocytes
AML
CHEMO M3: VitA
ALL
CHEMO PPx CNS
BM
Cytogenetics Prognosis Confirmatory Dx

3. Chronic Myelogenous Leukemia

- This is a disease of **matured** (chronic) **neutrophils** (Myelogenous) **cancer in the blood** (leukemia).
- It's associated with the **Philadelphia chromosome** – a t(9,22) translocation with overactive activity of a tyrosine kinase BCR-ABL.
- It presents as an **elevated white count** with an abnormal percentage of **neutrophils** (>60 WBC, >90% PMNs).
- Once the diagnosis is made confirm with a **Bone Marrow Biopsy**.
- Revolutionary therapy with the **tyrosine-kinase inhibitor Imatinib** has prolonged survival and delayed the **blast crisis**.
- Newer tyrosine kinase inhibitors have been used in imatinib-refractory cancers.
- However, inevitably this cancer becomes resistant, progresses to AML, and the patient ultimately succumbs.

4. Chronic Lymphoid Leukemia

- This is a disease of **mature** (chronic) **lymphocytes** (lymphoid) **cancer in the blood** (leukemia).
- It occurs in **old men** most commonly presenting as an **asymptomatic ↑ in WBC**.
- A **diff** will show an absolute lymphocyte count **>50.**
- You might see **smudge cells** (artificial rupture of fragile cells during smear preparation) on **smear**, but it's the diff and subsequent **bone marrow biopsy** that defines the disease.
- The average survival is about **ten years**.
- If they're old **do nothing**; they're more likely to die with it than from it.
- If they become symptomatic, treat with chemotherapy: **fludarabine** or **rituximab-based.**
- If the patient is young (<65) and there's a donor go ahead and perform a **stem cell transplant.**

Disease	*Patient*	*Age*	*Cell*	*1st Test*	*Best Test*	*Treatment*	*Special*
Acute	Fever, Bleeding, Petechiae, Infection, Pallor Bruising Bone Pain	7	Lymphoid	Smear	BM Bx > 20% Blasts	Ara-C MTX Cyclophosphamide Doxyrubicin	CNS PPx
		67	Myelogenous (Neutrophils)	Smear	BM Bx> 20% Blasts	Auer Rods/M3= Vit A Idarubicin + Ara-C	Auer Rods
Chronic	↑ White Count, Found on routine Screen	47	Myelogenous (Neutrophils)	Diff	BM Bx Philadelphia Chromosome t(9,22) BCR-ABL	Imatinib	Blast Crisis
		87	Lymphoid	Diff	BM Bx	If old or Donor = ∅ If old and symptomatic = Chemo If young and donor = BM Transplant	

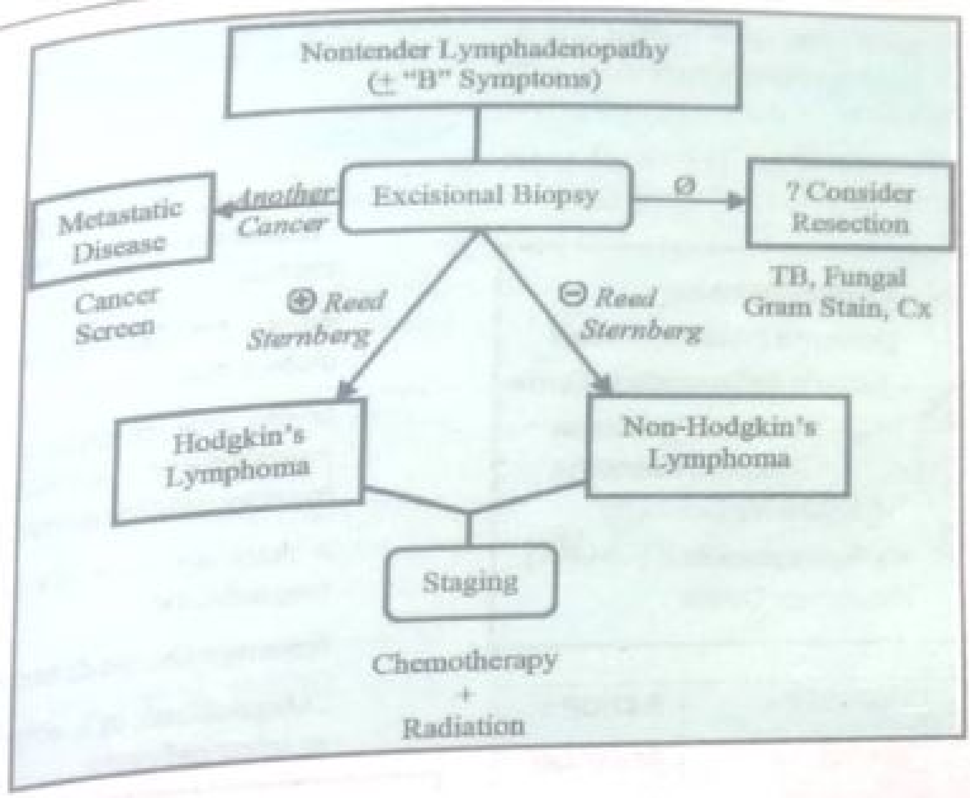
LYMPHOMA

Introduction

- Lymphoma is a malignancy of lymphocytes within lymph nodes.

Presentation and Diagnosis

- Lymphoma presents as **non-tender lymphadenopathy**.
- The presence of "**B symptoms**" (**fever, night sweats, weight loss**) is used only for staging designation.
- While it's true that B symptoms are more common in Hodgkins than Non-Hodgkins, it can be present in either disease and shouldn't be used to change the diagnosis.
- Other non-specific or uncommon findings are **Pel- Epstein fevers** that come and go over weeks or the **painful lymphadenopathy** with **EtOH** and **HSM**.
- These can be additive clues for a Hodgkin lymphoma, but aren't required for diagnosis or even suspicion of diagnosis.
- When a painless lymph node is encountered, the first step is to get an **excisional biopsy** (an **FNA** is insufficient and often equivocal).
- The excisional biopsy is required to see the lymph node architecture, giving evidence of the type of lymphoma as well as allowing detection of **Reed-Sternberg Cells**.
- The presence of these abnormal B cells defines Hodgkin's lymphoma versus Non Hodgkin's lymphoma. The excisional biopsy also allows for cytogenetic testing but that's beyond our scope. If it's negative for lymphoma consider mets and infection.


Nontender Lymphadenopathy
(± "B" Symptoms)
Excisional Biopsy
Another Cancer
Metastatic Disease
Cancer Screen
Ø
? Consider Resection
TB, Fungal
Gram Stain, Cx
⊕ Reed Sternberg
⊖ Reed Sternberg
Hodgkin's Lymphoma
Non-Hodgkin's Lymphoma
Staging
Chemotherapy
+
Radiation

Hodgkin	**Non-Hodgkin**
B Sxs more common	**No B Sxs**
Spreads **Anatomically**	**Non-Contiguous** Spread
Usually **IIa or better**	Usually **IIb** or **worse**
Pel-Epstein Fevers (rare)	**Extranodal** Disease
Chemo is **ABVD** and **BEACOPP**	Chemo is **R-CHOP** and **CNS prophylaxis** with **Methotrexate**

Staging

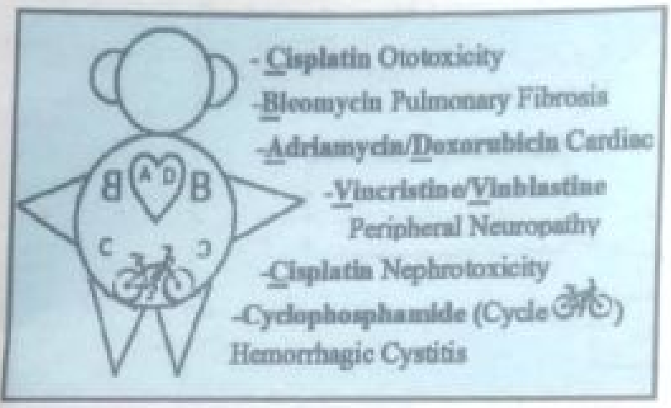
- Once the diagnosis of **"any lymphoma"** is made the next step is to **stage** the disease.
- For simplicity, once it's reached **> Stage IIb**, staging can stop.
- Start with a **Chest X-ray** then perform either a **Pet/Ct** or a **CT** of **Chest/Abd/Pelvis**.
- If everything is ***negative*** a **Bone Marrow Biopsy** must be performed to exclude bone marrow involvement.
- The push towards all Lymphoma receiving systemic chemotherapy has challenged the necessity for Bone Marrow aspiration, though it is still considered standard of care.

I	**One Group of lymph nodes**
II	**> One Group of lymph nodes on same side of diaphragm**
III	**> One Group of lymph nodes on opposite side of diaphragm**
IV	**Diffuse Disease in (blood or bone marrow)**

Treatment

- Lymphoma is treated with **chemotherapy and radiation** regardless of the stage.
- **Hodgkin's** is treated with **ABVD** in almost all instances except for extensive, bulky, or a disease presentation with poor prognostic features (you shouldn't learn what those things are for the test), in which case **BEACOPP** is used.

- **Non-Hodgkin's disease** is treated with **R-CHOP**, a Rituximab-based regimen or with Rituximab alone.
- Know the side effect profiles of these drugs using "Chemo man" to the right.

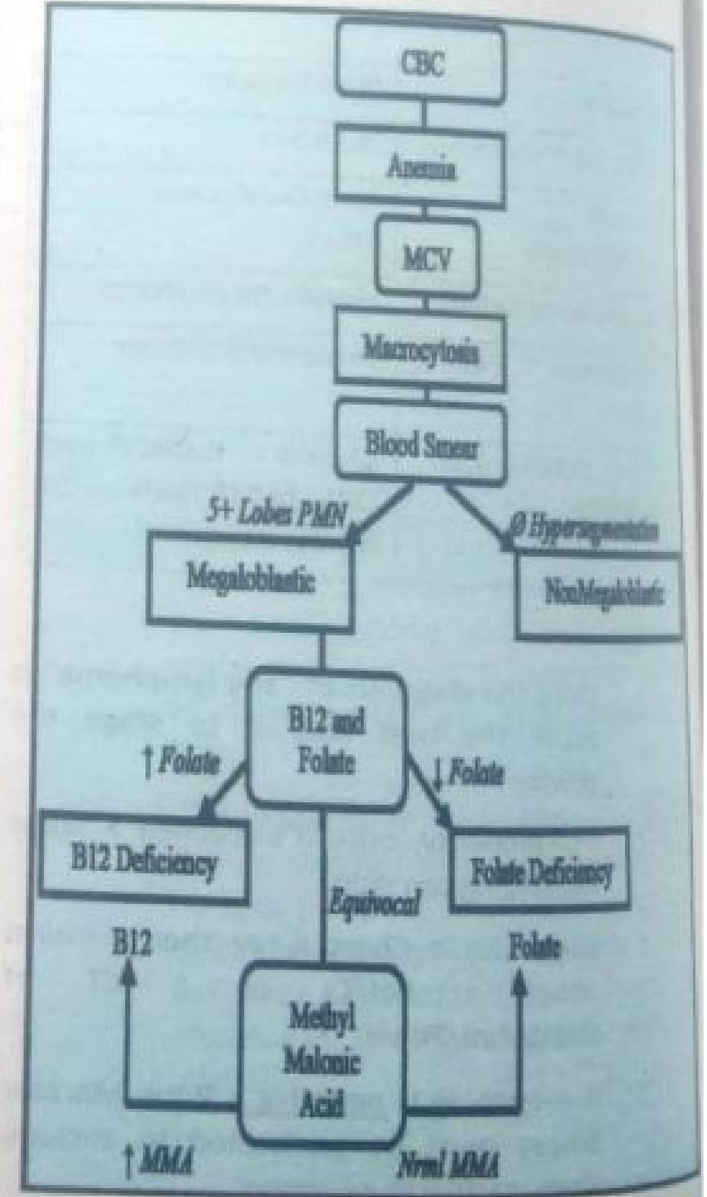

- Cisplatin Ototoxicity
-Bleomycin Pulmonary Fibrosis
-Adriamycin/Doxorubicin Cardiac
-Vincristine/Vinblastine Peripheral Neuropathy
-Cisplatin Nephrotoxicity
-Cyclophosphamide (Cycle) Hemorrhagic Cystitis
B
A D
B
C
C

ABVD =	BEACOPP =	R-CHOP =
Adriamycin/Doxorubicin	Bleomycin	Rituximab
Bleomycin	Etoposide	Cyclophosphamide
Vinblastine	Adriamycin/Doxorubicin	Hydroxydoxorubicin
Dacarbazine	Cyclophosphamide	Oncovorin / Vincristine
	Oncovorin / Vincristine	Prednisone
	Procarbazine	
	Prednisone	

MACROCYTIC ANEMIA

Introduction

- Macrocytic anemia is a production anem - reticulocytes will be reduced despite a anemia.
- When identified, the reflex test is th blood smear.
- In the case of impaired DNA synthesis (megaloblastic anemia) there'll be hypersegmented neutrophils.
- If there are none, it's said to be non megaloblastic.
- Nonmegaloblastic dz has some risk factors
- . Megaloblastic dz is either B 12 deficiency or folate deficiency.


CBC
Anemia
MCV
Macrocytosis
Blood Smear
5+ Lobes PMN
Ø Hypersegmentatio
Megaloblastic
NonMegaloblastic
B12 and Folate
↑ Folate
↓ Folate
B12 Deficiency
Folate Deficiency
Equivocal
B12
Folate
Methyl Malonic Acid
↑ MMA
Nrml MMA

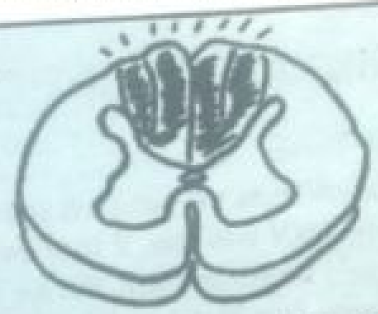
Folate Deficiency

- Folate comes from leafy greens and has small storage forms (3- 6 weeks) in the body.
- Thus, it often presents with higher acuity than B 12.
- Look for people who aren't eating real food - the chronic alcoholic or the elderly woman on a tea and toast diet.
- There aren't symptoms other than the anemia itself.
- A folate level will diagnose it and folate supplementation is usually sufficient for treatment.
- In equivocal cases where the folic acid levels are near normal, ancillary testing may be required.
- Donot remember the homocysteine levels - they're elevated in both Folate deficiency and B12 deficiency. Hence, not useful.
- The methylmalonic acid is unchanged in folate deficiency.
- Replace with oral supplementation.

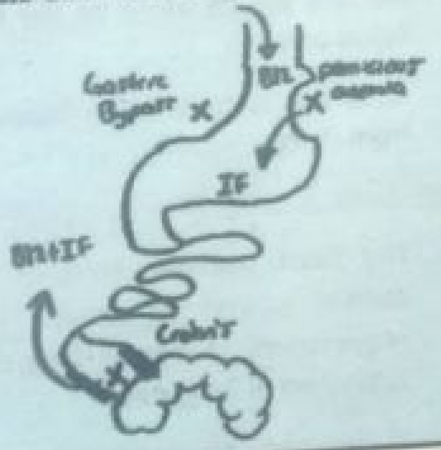
*Folate supplementation is performed in pregnancy to prevent neural tube defects in the fetus rather than to protect mom from anemia.

B12 Deficiency

- B 12 comes from animal products.
- It requires both intact parietal cells and an intact terminal ileum to be absorbed.
- The body has 3-10 years of stores it takes a long time to develop.
- The pathology is either decreased intake (strict vegans) or reduced absorption (as in those pernicious anemia, Crohn's disease involving the terminal ileum, and gastric bypass).
- It presents first with a megaloblastic anemia and then, if left untreated, with subacute combined degeneration of the cord.
- Diagnosis is made with a B12 level.
- If equivocal, an elevated methyl malonic acid is indicative of B12 deficiency. Don't use the homocysteine level to diagnose. The only time a Schilling test is done is when there's uncertainty about the etiology; it's rarely used. If the urine is positive for B 12, then there is no problem with absorption.
- Treatment is with B12 supplementation. If there's impaired absorption the supplementation must be intramuscular, else oral is sufficient.
- Be cautious with Folate administration. Throwing a lot of Folate at a B 12 deficiency can overcome the anemia, but it won't prevent neurologic symptoms.



Subacute Combined Degeneration of the cord.



Non-Megaloblastic Dz

- This isn't that interesting; there's just a list of things that cause it.
- It's important to first rule out a B12/Folate deficiency then look for: Liver Disease, EtOH, Medications (AZT, 5-FU, ARA-C) and metabolic conditions (Lesch-Nyhan, Hereditary Orotic Aciduria).

Dx	***Presentation***	***Pathology***	***Best Test***	***Homocysteine***	***MMA***	***Tx***	***Follow-up***
Folate Deficiency	Megaloblastic Anemia Only	Alcholic Maluutrition Leafy Greens, 3 weeks stores	↓ Folate Normal B12	Elevated	Normal	Folate	r/o B12
B12 Deficiency	Megaloblastic Anemia and Neuro Sxs (ANY), Peripheral Neuropathy (most common)	Pernicious Asemia, vegans Animal Products 3-10 year stores	Normal Folate ↓ B12	Elevated	Elevated	B12	Schilling's
Non-megaloblastic	After ruling out B12 and Folate look for Liver Dz/EtOH/Drugs/Metabolic						

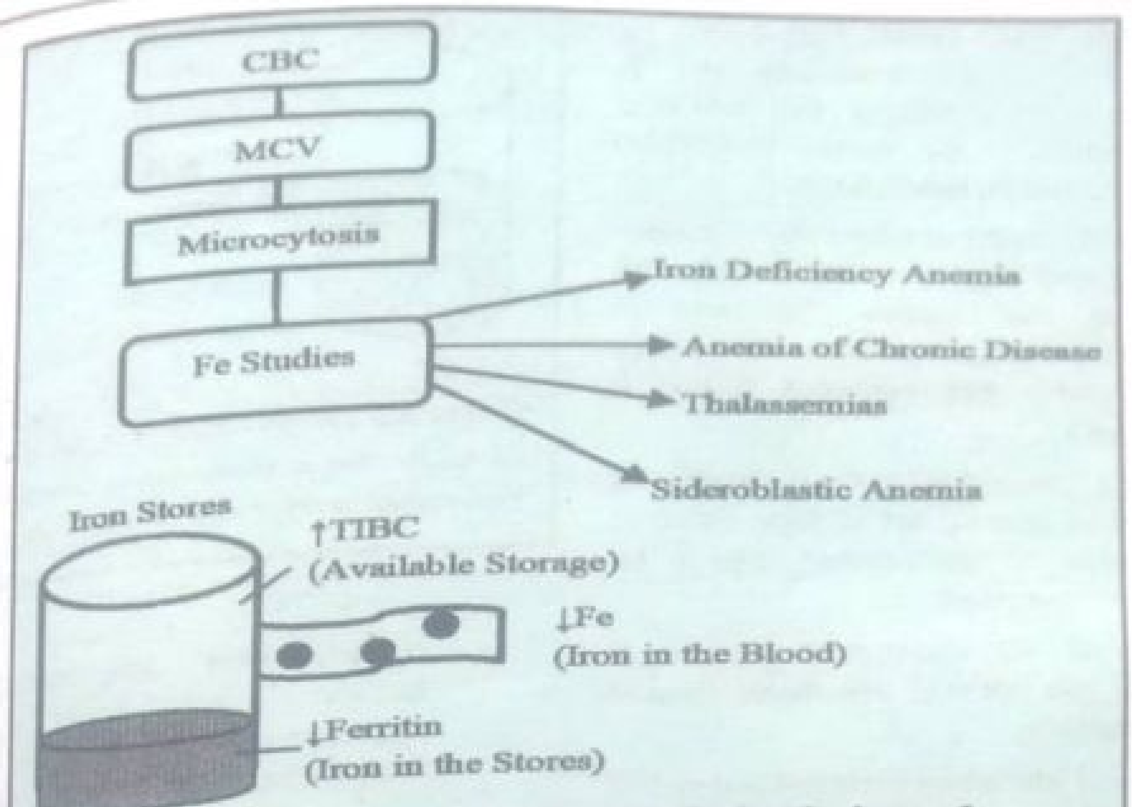
MICROCYTIC ANEMIA

Brief Introduction

- So we know the patient is anemic; we saw the **MCV was low**. If they were **unstable** we'd **transfuse** them. But we ought to get some labs first because after transfusion the labs will be based on the transfused blood only.
- Step one is to get **Iron Studies** and go from there.

Iron Deficiency Anemia

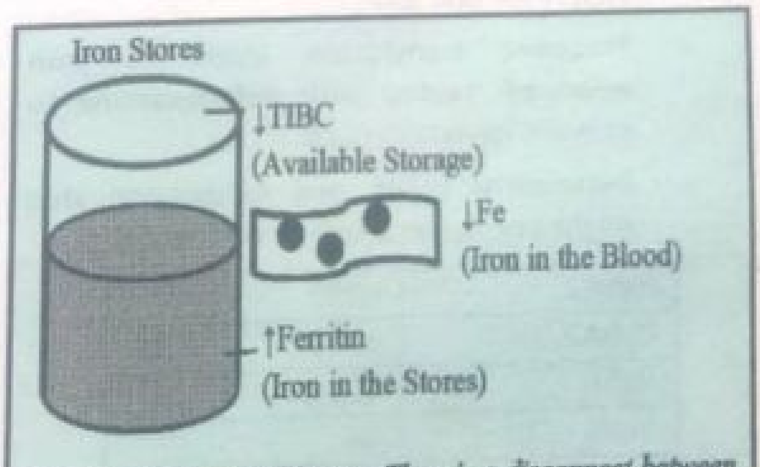
- The **most common** form of microcytic anemia is iron deficiency. The normal requirement of iron is **1mg/day** with a maximum of **3mg/day**.
- If the body starts to lose blood it may begin using iron (to replace the lost hemoglobin) at a greater rate than it can be absorbed. But this also means that it must be a **chronic** source of blood loss.
- Potential causes are **GI Bleeds** (slow, polyps, hemorrhoids, etc) or **Gynecologic losses** (menorrhagia, cancer).
- Alternatively, decreased uptake of iron in a non-bleeding person (as in a **gastrectomy**) is possible.
- In any male or postmenopausal female with iron deficiency anemia follow up with a **colonoscopy** to rule out cancer.
- The **best** test to diagnose iron deficiency anemia is a **Bone Marrow Biopsy.** But it's rarely done because Iron studies are so good at diagnosing Iron Deficiency Anemia.
- The most sensitive part of the iron studies is a **low Ferritin** (if Ferritin is low, it's iron deficiency anemia, period). That is, the **iron stores** are small.
- Low stores means high **capacity** to bind, so there'll be an **elevated TIBC**.
- The low stores also means **low serum iron**.
- Stop the bleeding then **give iron**.
- It takes **6 weeks** to replace the **serum iron** and **6 months** to replace **iron stores**.


CBC
MCV
Microcytosis
Fe Studies
Iron Deficiency Anemia
Anemia of Chronic Disease
Thalassemias
Sideroblastic Anemia
Iron Stores
↑TIBC
(Available Storage)
↓Fe
(Iron in the Blood)
↓Ferritin
(Iron in the Stores)

Iron Deficiency Anemia. *Iron stores are depleted, plenty of storage availability. Iron is low. ↑TIBC, ↓Ferritin, ↓Fe.*

Anemia of Chronic Disease

- When there's **inflammation** the body is trying to prevent whatever it's fighting from getting the iron it needs.
- If it's only an acute process, that helps fight infection.
- A side effect is that it makes the iron unavailable even to the host.
- Great in fighting an infection; awful in a **chronic disease**.
- Essentially, what happens is the connection between the iron stores and the blood is severed.
- The body has **a lot of iron stored** so a **low capacity to bind** but still has a **low serum iron**.
- Treating the underlying disease will fix the anemia (the inflammation goes away, the iron stores can be reconnected to the blood).
- Sometimes, that's not possible (Lupus, Rheumatoid Arthritis) so help the body utilize iron stores with **EPO**.


Iron Stores
↓TIBC
(Available Storage)
↓Fe
(Iron in the Blood)
↑Ferritin
(Iron in the Stores)

Anemia of Chronic Disease. *There's a disconnect between the blood and the iron stores, but iron absorption is intact. ↓TIBC, ↑Ferritin, ↓Fe*

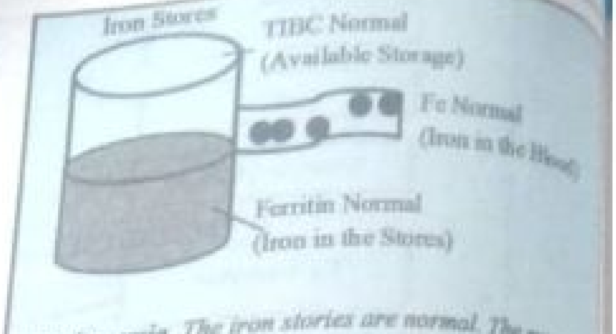
Thalassemia

- Something different is going on in thalassemia.
- It's not the iron stores that are the problem - it's the **hemoglobin**.

- There's a genetic disease (α, chromosome 16, frameshift and β, chromosome 11, deletion) that leads to ↓ production of the normal hemoglobin with 2α and 2β; **HgbA1 $\alpha 2\beta 2$.**
- **It doesn't matter which portion is broken - the patient is going to have anemia with normal iron studies.** The way to definitively diagnose thalassemia is with a **Hemoglobin Electrophoresis** (α-thal is 'normal').
- Here's the kicker; because anemia is based on severity, not etiology, definitive diagnosis is not required except for genetic counseling.
- *Think of ALL thalassemia patients as **minor** (do nothing) and **major** (routine transfusion).*
- *The deal with which hemoglobin it is, 1, 2, 3, 4 gene deleted is unnecessary and bogus for the clinical rotations.*
- *Recognize the hemoglobins (A1, A2, Fetal, Barts, HbH) but realize it's either **do nothing** (minor) vs **transfuse** (major).*
- *Each bag of blood has **350mg Fe** - enough supply for one year.*
- *Frequent transfusion leads to **iron overload** treated with **deferoxamine** to prevent Hemosiderosis.*
- *Deferasirox is an oral medication that might pop up on a test or on the wards.*

HgbA1	$\alpha 2\beta 2$
HgbA2	$\alpha 2\delta 2$
HgbF	$\alpha 2\gamma 2$
Barts	$\gamma 4$
HgbH	$\beta 4$

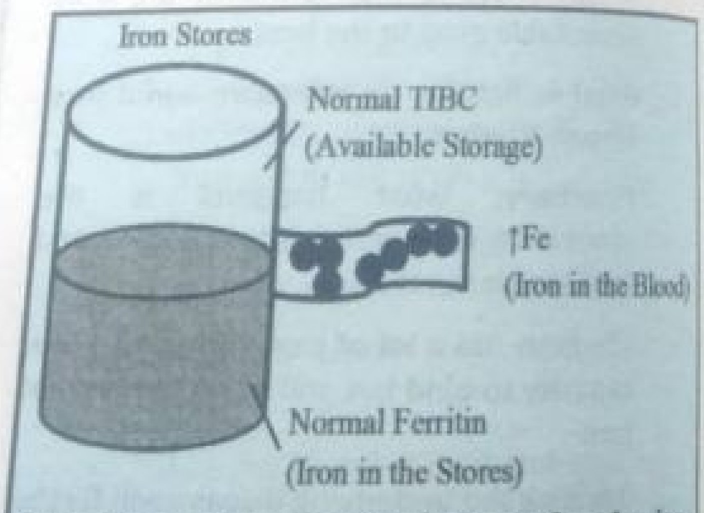
	â-Thal	*á-Thal*
Asx	**N/A 1**	**Gene Deleted**
Minor	***1 Gene Deleted***	***2 Gene Deleted***
ajor	***2 Gene Deleted***	***3 Gene Deleted***
ead	***N/A***	***4 Gene Deleted***



***Thalassemia.** The iron stories are normal. The more ge deleted, the more severe the disease. Consider Thalassemias as either minor or major only.*

Sideroblastic Anemia

- Nobody likes Sideroblastic anemia because it's "hard." Really it's because i sounds terrifying and is named from wha it **looks like on Bone Marrow Biopsy**.
- It's the only microcytic anemia wi **elevated iron**. Definitively diagnose it wi a **bone marrow biopsy**, which will show the **ringed sideroblasts**.
- It has a number of causes (**Lead**, EtOH **Isoniazid**, a pyridoxine metabolic disease of **B6**, and **Myelodysplasia / AML**).
- Get the pt away from lead, give them B6 and do a **BM Bx** for the cancer (which coincidentally, you just did for the diagnosis).



***Sideroblastic.** Diagnosis of Exclusion confirmed on bone marrow biopsy. The tipoff is an **elevated** iron despite an anemia with small cells*

Anemia	*Pathology*	*Ferritin*	*TIBC*	*Iron*	*Best Test*	*Tx*	*f/u*
Iron Deficiency	Blood Loss (Chronic) GI, GYN	**↓Ferritin**	**↑TIBC**	**↓ Fe**	BM Bx	Iron	**Colonoscopy**
Anemia of Chronic Disease	Any chronic inflammatory disease	**↑Ferritin**	**↑TIBC**	**↓ Fe**	BM Bx	**Treat the Dz (Steroids) Try Epo**	-
Thalassemia	Chr 16, α, Frameshift Chr 11, β, Deletion	Normal Ferritin	Normal TIBC	Normal Iron	**Hgb Electrophoresis**	Minor: Ø Major: Transfuse	**Deferoxamine** (transfusions)
Sideroblastic	Lead, B6, genetic Dz, Myelodysplasia, EtOH, ↓ Copper	Normal Ferritin	Normal TIBC	**↑ Fe**	BM Bx **(Ringed Sideroblasts)**	Give B6, Look for Cancer	

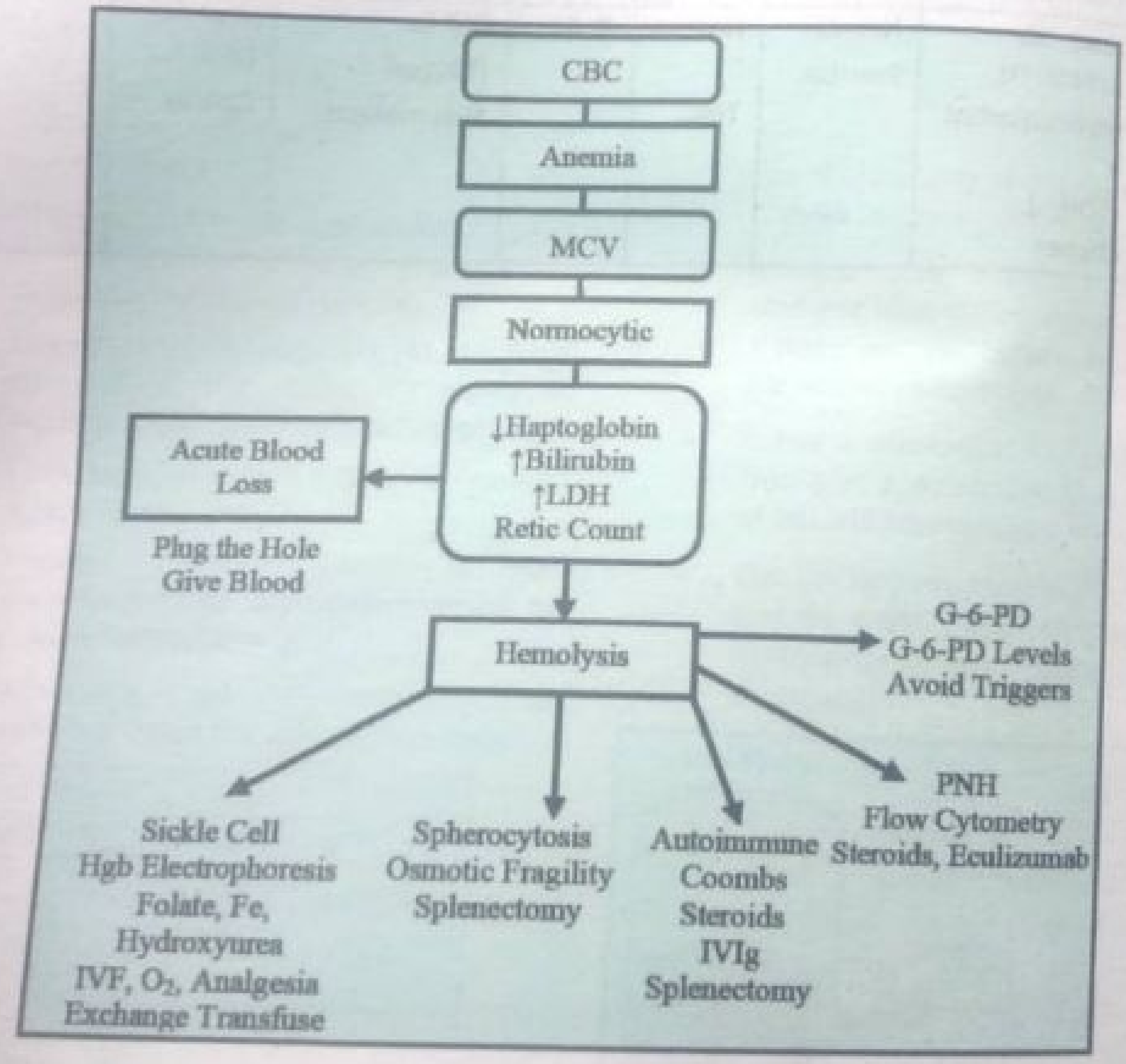
NORMOCYTIC ANEMIA

Introduction

- When it comes to normal sized anemia there are generally two things to consider: **hemorrhage** and **hemolysis**.

Anemia of Acute Blood Loss

- When the blood loss is acute there's an **acute drop in H/H**.
- This generally has an obvious sour (trauma, GI, GYN) and isn't the sl chronic onset iron deficiency stuff.
- An underlying anemia **can be expos** with dilution, but you **can't dilute** **normal person's** H/H to anemia.
- If a Normocytic anemia is revealed, loo for the source of the loss.
- Fix this by **plugging the hole** and/or giving blood.


CBC
Anemia
MCV
Normocytic
↓Haptoglobin
↑Bilirubin
↑LDH
Retic Count
Acute Blood Loss
Plug the Hole
Give Blood
Hemolysis
G-6-PD
G-6-PD Levels
Avoid Triggers
PNH
Flow Cytometry
Steroids, Eculizumab
Sickle Cell
Hgb Electrophoresis
Folate, Fe,
Hydroxyurea
IVF, O2, Analgesia
Exchange Transfuse
Spherocytosis
Osmotic Fragility
Splenectomy
Autoimmune
Coombs
Steroids
IVIg
Splenectomy

Hemolytic Anemia

- Red blood cells last 120 days.
- When they die they release iron and hemoglobin into the blood.
- **Haptoglobin** binds up hemoglobin for transport to the liver.
- Because it's bound to hemoglobin ("used up") it'll be ↓ in hemolysis.
- There will be an overwhelming of the conjugation system so there will also be an **indirect hyperbilirubinemia** causing **jaundice, icterus**, and **pruritus**.

- There can be a lot of talk of intravascular vs extravascular hemolysis but let's focus on identifying the diagnosis and management rather than the basic science details.

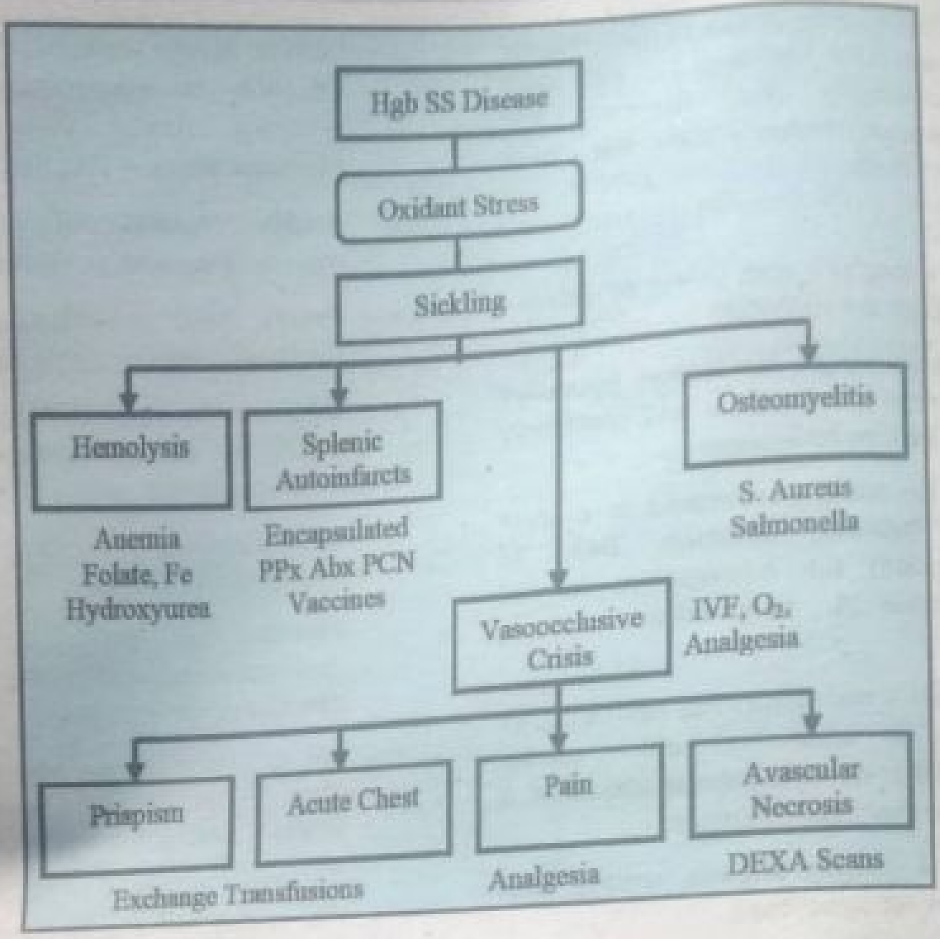
Sickle Cell Anemia

- This is a long one with plenty of details - all of which are important.
- It's caused by an **Autosomal Recessive** mutation in the **β-Globin** and commonly seen in **African Americans.**
- When the patient undergoes an oxidant stress (**hypoxia, infection, DKA,** or **dehydration**) the hemoglobin, termed **Hemoglobin S, polymerizes** inducing **sickling.**
- It creates a non-deforming cell that gets trapped in capillaries, which causes **hemolysis** and **microvascular occlusion.** It results in many consequences.
- One is a **chronic anemia,** usually with sufficient reticulocytosis.
- If the retic is low, consider either an **acute aplastic crisis** (parvovirus 19) or a **folate deficiency.**
- For this reason HbSS patients should be on **daily folate + Fe.** Another consequence is the **vasoocclusive crisis.** Microvascular occlusion causes infarction.
- Infarction hurts.
- These people will be on **chronic pain management** because their joints hurt all the time.
- Occasionally, they'll suffer an acute crisis where they need **IVF, O2,** and **Analgesia** to ride out the attack.
- If the patient develops an acute chest (ARDS picture) or priapism, they need an **exchange transfusion** to get over the severe crisis.
- But infarction costs them more than that.
- **Splenic Autoinfarction** increases risk for **infection** by **encapsulated organisms,** requiring **annual vaccinations** (PCV, Meningococcus, H. Flu, HBV).
- **Aseptic Necrosis** of the hip/femur requires **dexa scan** screening.
- Finally, these patients are at **↑Risk** for **salmonella osteomyelitis.**
- Decrease the amount of bad hemoglobin (HbSS) by giving **Hydroxyurea** (induces fetal hemoglobin, which does not sickle).
- Prevent sickling by avoiding stressors and staying hydrated.
- Control the pain with **analgesia** chronically and reduce the anemia with Iron and Folate.
- But how do we know who has sickle cell disease? Seeing **sickled cells** on a **blood smear** is sufficient for the diagnosis.
- Definitive diagnosis of the disease or of the carrier state may be confirmed by **Hemoglobin Electrophoresis.** Finally, the carrier state almost never sickles unless under extreme conditions (such as climbing Mount Everest) and in the **renal vein** (↑ risk for renal vein thrombosis).

ii. G6PD Deficiency

- An X-linked genetic disorder prevalent in **Mediterranean ancestry** presenting with a hemolytic anemia after exposure to oxidant stress: **drugs** (dapsone, primaquine), **infection, DKA,** or **foods** (fava beans).
- Diagnose it with a **smear** showing **Heinz Bodies** and **Bite Cells.**
- Confirm the diagnosis with a **G-6-PD level** but do it weeks after the attack (doing so too soon may be artificially normal).

> The Greek man eating dapsone for breakfast, primaquine for a lunch, fava beans for dinner, and a bucket of sugar for dessert (to go into DKA) might have a G6PD deficiency


Hgb SS Disease
Oxidant Stress
Sickling
Hemolysis
Anemia
Folate, Fe
Hydroxyurea
Splenic Autoinfarcts
Encapsulated
PPx Abx PCN
Vaccines
Osteomyelitis
S. Aureus
Salmonella
Vasoocclusive Crisis
IVF, O2,
Analgesia
Priapism
Acute Chest
Exchange Transfusions
Pain
Analgesia
Avascular Necrosis
DEXA Scans

III. Hereditary Spherocytosis

- The cytoskeleton of the RBC is missing a piece (usually **spectrin** or **ankyrin**, band 3.1 or pallidin). This presents just like a hemolytic anemia.
- The **spherocytes** can be seen on a **smear**, though they aren't pathognomonic.
- Confirm the diagnosis with an **osmotic fragility** test.
- Because the big bad spleen beats up on the little spherocytes a **splenectomy** will stop the anemia. However, the cells will persist as spheres.
- Splenectomy has its own problems so stick with **Folate** supplements unless it's really severe.

Iv Autoimmune Hemolytic Anemia

- As the name implies, it's an **autoimmune disease** that attacks RBC. There can be **cold AIHA** caused by **Mycoplasma** and **Mono**, which produces **IgM** against RBC a cold temperatures.
- Avoid the cold and it's not a problem.
- **Warm AIHA** is caused by **autoimmune disease** (any Rheumatic disease), **drug** (PCN, Sulfa, Rifampin), and **Cancer**, producing **IgG** against RBC at warm temps. Treat this like any autoimmune disease by giving **steroids**, **IVIg** when acute, and **splenectomy** if refractory. The **smear** is non-diagnostic; the **Coombs** test *is* diagnostic.

Smear = Schistocytes, Helmet cells (not pathognomonic)

v. Paroxysmal Nocturnal Hematuria

- Caused by a mutation in the **PIG-A** gen the red blood cells have no **GPI-Anchor** so they can't inhibit complement fixation.
- Fixation occurs all the time, but accelerated by **hypoxia** (when you sleep)

- So, while these patients sleep complement fixes, cells **lyse,** and they **wake up with hematuria.**
- They can also get **venous thrombosis** in intra-abdominal veins causing **abdominal pain.** Confirm the diagnosis with a **flow cytometry** and treat with **Anti-Ab Drugs** (eculizumab).

Flow cytometry shows absence of CD55 + CD59

Disease	*Patient*	*Path*	*1st Test*	*Best Test*	*Treatment*
G-6-PD Deficiency	Mediterranean man who eats dapsone, primaquine, fava beans, and goes DKA	G6PD Deficiency, cannot tolerate oxidative stress X-Linked	Smear **Heinz Bodies Bite Cells**	**G-6-PD Levels** weeks after the attack	Avoid Oxidant Stress
Hereditary Spherocytosis	Enlarged Spleen	Defective RBC structural proteins, Splenic Destruction	Smear (Spherocytes)	**Osmotic Fragility**	**Splenectomy** (Spherocytes Remain)
Autoimmune Hemolysis	IgG: Drugs, Cancer, Rheum IgM: Mycoplasma, Mono	Autoimmune Antibodies	Smear (Spherocytes)	**Coombs Test**	Steroids, IVIg, **Splenectomy**
Paroxysmal Nocturnal Hematuria	Irregular bouts of morning hematuria and abdominal pain	PIG-A gene mutation, failure to inhibit compliment on RBC	-	**Flow Cytometry**	Steroids, Eculizumab
Sickle Cell Disease	African American, chronic pain, acute chest, priapism	Hgb S polymerizes in response to stress	Smear (Sickles)	Hgb Electrophoresis	IVF, O2, Analgesia, Exchange Transfusion

PLASMA CELL CANCERS

Multiple Myeloma

- Multiple Myeloma is a dysfunction of plasma cells, which normally secrete **Immunoglobulins** in response to antigen presentation.
- In multiple myeloma the plasma cells secrete one antibody against some phantom antigen.
- This dedicates the entire immune system to fighting something that doesn't exist. There are multiple consequences.
- The first is the **monoclonal antibody** produces overwhelming concentration of useless antibody.
- It can be detected by **Hgb Electrophoresis (Spep)** as an **M spike**.
- The consequence is when real infection comes there's antibodies to fight

infection; these patients develop **recurrent infections.**

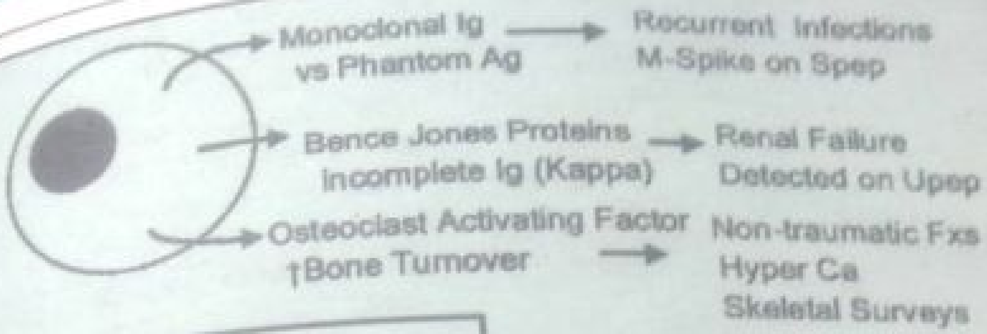
- Sometimes complete Ig aren't made, but rather only pieces.
- They get deposited in the kidneys and can be detected on **Urine Electrophoresis (Upep).**
- The fact that there are these proteins in the blood (both intact Ig + Bence Jones) means there will be an **elevated protein gap.**
- Any time there are antibodies being made (HIV, Viral, bacterial infection) the protein **gap** can increase, but a sustained **elevation** on routine labs may be a tipoff.
- Plasma cells also secrete **osteoclast activating factor** which causes the bone resorption to go crazy.
- It results in **hypercalcemia** and frail bones - = **pathologic non-traumatic fractures** especially in the **elderly.** So patients will be **old,** with **weird fractures, renal failure, hyper Ca,** and an **↑Protein Gap.**
- The first thing to do is an **Spep** for the **Mspike** and a **Upep** for Bence Jones.
- A **Bone Marrow Biopsy** must show a **>10% Plasmacytosis.**
- **A skeletal survey** is used to assess for lytic lesions (owing to the lytic nature of this disease, a bone scan, used to assess for boney metastasis of other cancers can't be used).
- Treatment options are dependent on the **age;** if **<70 + Donor** do a **stem-cell transplant** after chemo. For **>70** or **No Donor** do chemo only.
- Chemotherapy is often with Melphalan, Prednisone and either Thalidomide or Bortezomib.

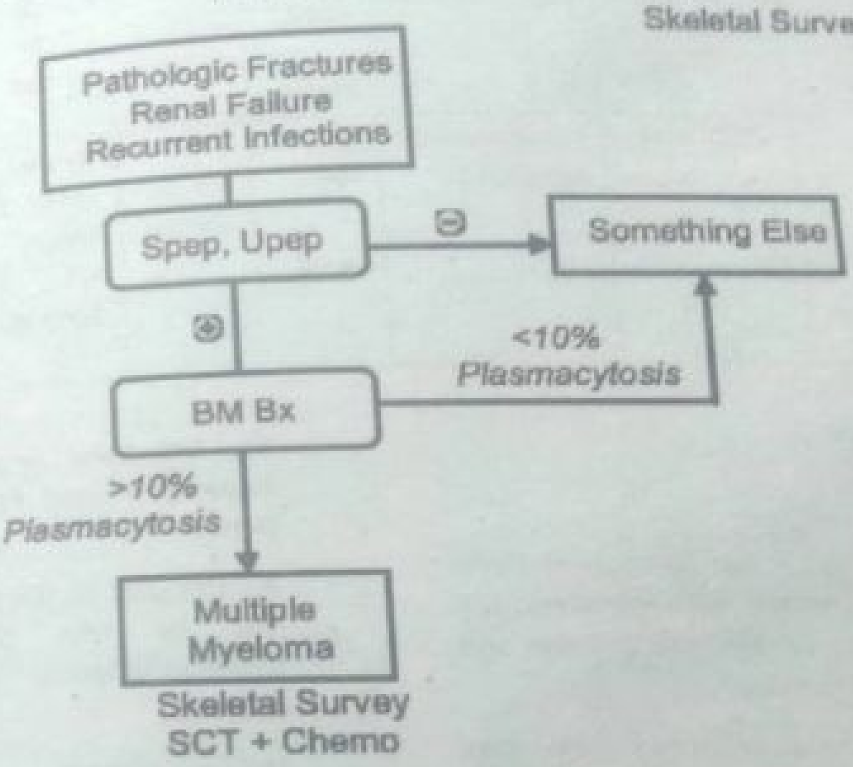
Monoclonal Gammopathy of Uncertain Significance

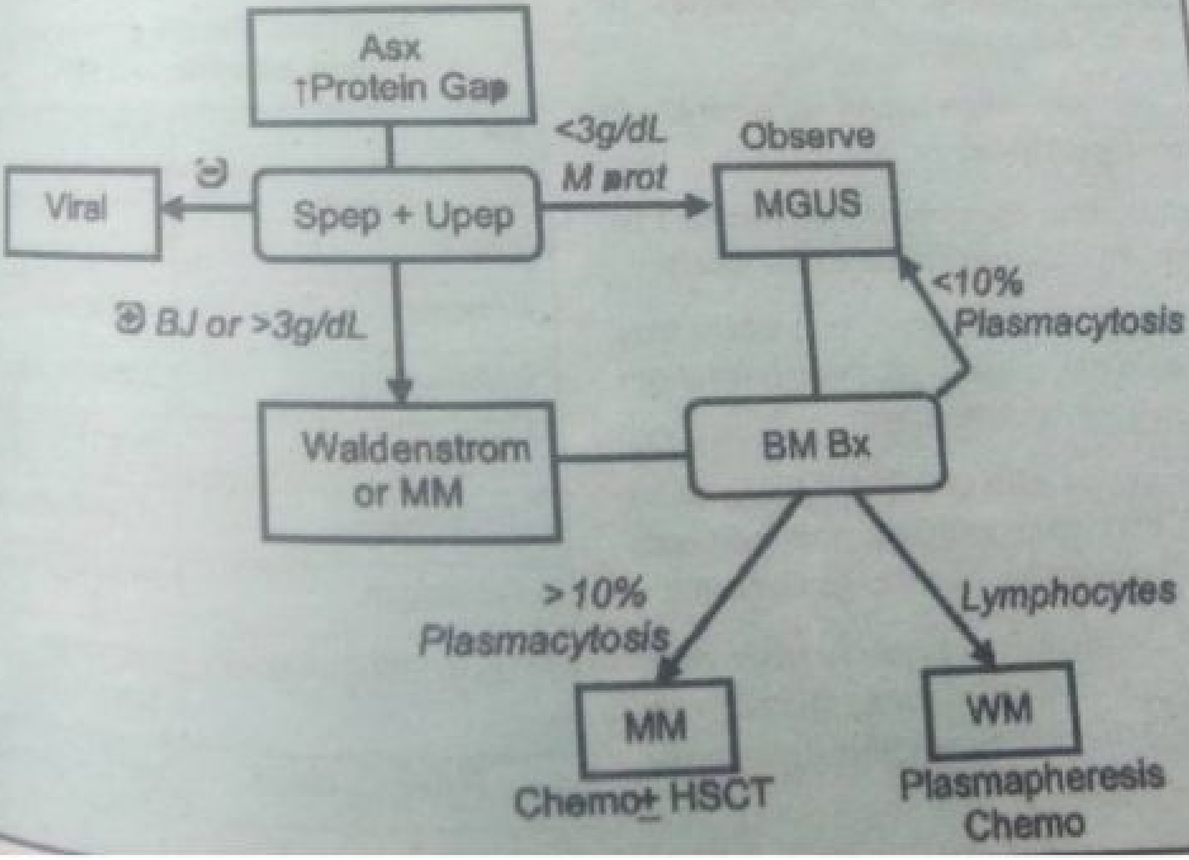
- MGUS is when there's a **+Spep** but without **Bence Jones, Lytic Lesions, Renal Failure, HyperCa** and a **plasmacytosis < 10%.**
- Do everything to rule out multiple myeloma, but then just monitor for conversion to multiple myeloma (~2% / year).
- This probably represents an early version of MM, but the patients who acquire it are often quite old and often do not require any treatment.

Waldenstrom's Macroglobulinemia

- This is a myeloma-spectrum disorder that presents quite differently than myeloma.
- The marrow secretes **IgM** rather than IgG. Thus, it presents with **peripheral neuropathy** and **hyperviscosity syndrome** rather than renal failure and bone fractures. This too will have an elevated M-Spike on Spep, but will lack the lytic lesion on skeletal survey.
- **Bone Marrow Biopsy** shows **Lymphoplasmacytic Lymphoma** in more than 10% of the marrow. This disease is often **left alone if asymptomatic** and elderly. **Treatment** for hyperviscosity syndrome requires **plasmapheresis.** This is treated more like a **lymphoma** than a plasma cell dyscrasia; the **chemotherapeutic regimen** mirrors Non-Hodgkin's Lymphoma **with the** use of **Rituximab-containing-regimens.** Diagram


Monoclonal Ig
vs Phantom Ag
Recurrent Infections
M-Spike on Spep
Bence Jones Proteins
Incomplete Ig (Kappa)
Renal Failure
Detected on Upep
Osteoclast Activating Factor
↑Bone Turnover
Non-traumatic Fxs
Hyper Ca
Skeletal Surveys


Pathologic Fractures
Renal Failure
Recurrent Infections
Spep, Upep
⊖
Something Else
⊕
<10%
Plasmacytosis
BM Bx
>10%
Plasmacytosis
Multiple
Myeloma
Skeletal Survey
SCT + Chemo


Asx
↑Protein Gap
<3g/dL
M prot
Observe
MGUS
⊖
Viral
Spep + Upep
⊕ BJ or >3g/dL
<10%
Plasmacytosis
Waldenstrom
or MM
BM Bx
>10%
Plasmacytosis
Lymphocytes
MM
Chemo± HSCT
WM
Plasmapheresis
Chemo

Disease	*Minor Sxs*	*Major Sxs*	*1st*	*Best*	*Follow Up*	*Treatment*
Multiple Myeloma	Hyper Ca Renal Failure Anemia	Nontraumatic Fx in the elderly ↑ Protein Gap	⊕ Spep ⊕ Upep	BM Bx >10% plasma	Skeletal Survey	<70 + Donor = Chemo + HSCT >70 or Donor = Chemo
MGUS	Ø	Ø	⊕ Spep, – Upep	BM Bx >10% plasma	Annual Screen for MM	Observe
Waldenstrom's Macroglobulinemia	Peripheral Neuropathy	Hyperviscosity Syndrome	⊕ Spep, – Upep	BM Bx >10% plasma	Serum Viscosity Nrml = 1.8, Abnormal >5-6	Plasmapheresis for Hyperviscosity Chemotherapy ± HSCT

THROMBOCYTOPENIA

Disseminated Intravascular Coagulation

- At its core, DIC is the function of **fibrin clots** that consume both **platelets** and **factors**, which causes both a factor and platelet type bleeding.
- Blood shearing across those fibrin clots produces **microangiopathic hemolytic anemia (MAHA)** and **Schistocytes** on smear.
- Clots and inflammation in general can produce a **fever**.
- Clots occur everywhere they shouldn't be and then can't form where they should.
- Thus, the patient bleeds (not where they should be), but also get thrombosis (from where they shouldn't bee).
- The person who gets DIC is going to be sick from something else, and then ends up dropping their platelets and bleeding.
- Because these are caused by **fibrin clots,** fibrinogen is consumed, factors are chewed up, and there's also a rise in the split products.
- The **DIC panel** reveals **low fibrinogen, elevated PT and PTT**, and **elevated D-Dimer**.
- It's this part of the panel that separates DIC by labs (the presence of thrombocytopenia and schistocytes doesn't).
- The underlying condition must be corrected to reverse DIC. In the meantime, give the patient what's missing – **Blood, platelets, and FFP.**

DIC	*TTP*
Sick already, then bleeds	Normal, then FAT RN
↓ Platelet	↓ Platelet
Schistocytes	Schistocytes
↑ PT/ PTT	Nrml PT/PTT
↑ D-Dinner	Nrml D-Dinner
↓ Fibrinogen	Nrml Fibrinogen
Reverse underlying Dz	Exchange Transfusion
Give Platelets, blood	NEVER give platelets

Thrombotic Thrombocytopenic Purpura

- TTP is an **autoimmune** disease where clots form - just like in DIC.
- But these clots are **hyaline** clots that **don't** consume factors, fibrinogen, or platelets.
- **ADAMTS-13** is deficient.
- It fails to cleave vWF multimers, which persist and **swallow platelets**.
- The thrombocytopenia has nothing to do with the clots, but with these large vWF multimers (at least we think).
- There's a classic **pentad** for TTP, with the mnemonic **FAT RN**.
- There's Fever, Anemia, Thrombocytopenia, Renal Failure, and Neurologic symptoms that wax and wane.
- Diagnosis is based on a **normal DIC panel** despite **thrombocytopenia** and **anemia**. Schistocytes may be present.
- The Laboratory diagnosis separates them.
- For TTP, **NEVER** give platelets (it'll worsen the MAHA).
- Instead, do a **plasma exchange** (take out the antibodies and give back plasma with a lot of ADAMTS-13), or a **plasma transfusion** (give ADAMTS-13 only).

Idiopathic Thrombocytopenic Purpura

- ITP is an **autoimmune** disease of an unknown etiology that's a **diagnosis of exclusion**. Look at every other cause first, including **bone marrow biopsy**.
- Once exhausted, it's the diagnosis.
- The treatment is **steroids** (long term low dose better than short term high dose as the patient remains sensitive to treatment), though **IVIg** can be started acutely to get platelets up faster.
- If steroids fail, a **splenectomy** is definitive.
- If splenectomy fails or is **contraindicated**, the remaining option is **Rituximab**.

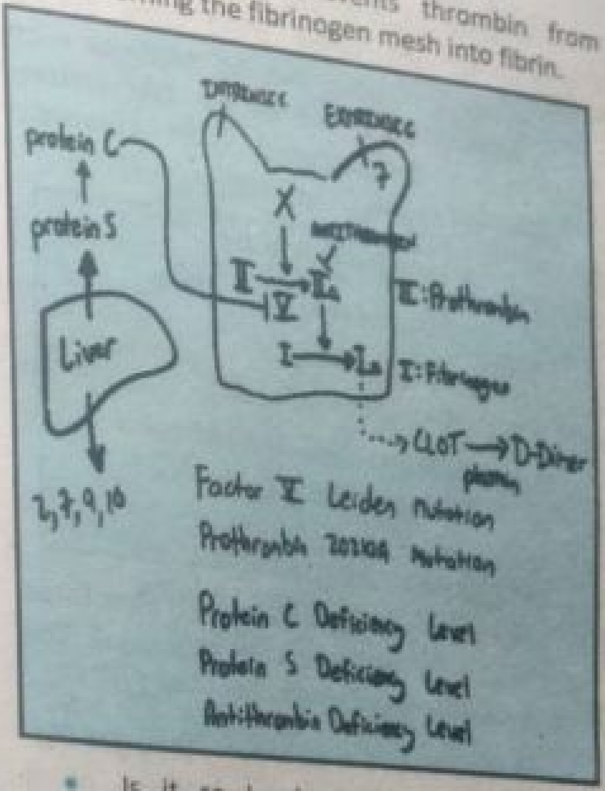
Heparin-Induced Thrombocytopenia

- If the patient is on **any heparin** there may be an **autoimmune destruction** of platelets, typically occurring at day 4-10 (earlier if second exposure).
- **Stop the heparin**, start **Argatroban**, and then send out the HIT panel. Treatment before diagnosis in this case.

THROMBOPHILIA

The (Anti) Clotting Cascade

- **Protein S** activates **Protein C**.
- **Protein C** binds to **Factor V** to inactivate it, reducing the production of Thrombin from Prothrombin.
- **Antithrombin** prevents thrombin from turning the fibrinogen mesh into fibrin.


INTRINSIC
EXTRINSIC
protein C
protein S
Liver
2,7,9,10
X
7
ANTITHROMBIN
II
V
IIa
I
Ia
II: Prothrombin
I: Fibrinogen
CLOT → D-Dimer
plasmin
Factor V Leiden Mutation
Prothrombin 20210A Mutation
Protein C Deficiency Level
Protein S Deficiency Level
Antithrombin Deficiency Level

- Is it so hard to imagine if there's a **deficiency** in **Protein C**, **Protein S**, or **Antithrombin** that there'd be an unusual amount of clotting? What if factor V just didn't get the Protein C message? Say there was a mutation of Factor V that made it resistant to the activity of protein C. That's **Factor V Leiden** - the most common thrombophilia. Don't forget about **Prothrombin 20210A**. These are the named thrombophilias that you should be able to recognize that you should be able to recognize.

- They're all genetic diseases that require genetic testing to diagnose. They can all be treated **with coumadin (Warfarin).** They're all related to factor clotting so induce anti-clotting with coumadin to counteract the anti-clotting-deficient endogenous system. Read that again to make sure you got it. But wait! Doesn't Coumadin inhibit the production of clotting factors and proteins from the liver? Coumadin first **inhibits protein C and S,** actually INCREASING clotting when it's begun. That's why it'simperative to always start with a **Heparin Bridge**. It'll revent the whole thing from getting started. Heparin can be removed once proteins C, S, and all the liver clotting factors are depleted (with Coumadin being left on).

For the resident, order:

- Protein C Levels
- Protein S Levels
- Prothrombin levels
- Antithrombin 20210A Mutation
- Factor V Leiden Mutation
- Antiphospholipid Assay

- But what's the right time to go after these tests and to treat with Warfarin? The answer is never.
- If the person has **two clots, they get life-long anticoagulation** regardless of a genetic defect or not. You suspect genetic susceptibility when there are multiple unprovoked DVTs.... and you would be anticoagulated for life anyway.
- If the person wants to STOP anticoagulation, genetic testing needs to be performed to assess the risk of being off it. Otherwise, they're all treated the same way.

Antiphospholipid Antibody Syndrome APLA / APS

- This diagnosis warrants special mentio
- Caused by the **lupus anticoagulant** (whic is frustrating because it's a procoagulan in vivo), the patient will present wi **autoimmune disorders** and **bleedin** They'll have both **arterial AND venou thrombosis;** it may also present with a history of early miscarriages.
- The goal INR is 2-3 for initial therapy.
- Repeat clot on warfarin indicates a rise in the goal INR.

INFECTIOUS DISEASE

ANTIBIOTIC LADDER

Introduction

- The bugs that cause disease largely stay the same; the antibiotics that treat them don't.
- Case in point, Staph aureus was the **most common cause of osteomyelitis** 50 years ago and still is today.
- Abx Resistance means the drugs to treat are constantly evolving.
- In general, **start with penicillin**. It's a cidal (kills bacteria) and typically successful.
- There are two pathways from there - those that cover **staph** and those that cover **gram negative rods**.

Staph

- The Methicillins (oxacillin, cloxacillin, dicloxacillin, and nafcillin) are very good at killing staph.
- Unfortunately, they're all really good at **making MRSA**. When sensitive to methicillin, any of the –cillins should be used. In general, this **isn't empiric**.
- **Vancomycin** is the typical drug used for empiric coverage of Staph. It covers MRSA. However, just because it's a "big gun" doesn't imply it has broad coverage – it's weak against everything else.
- **Linezolid** is top of the line. It's the last resort for Vancomycin resistant Enterococcus (VRE) or Staph (VSA). Use this sparingly - resistance to this means there's nothing left.

Gram Negatives

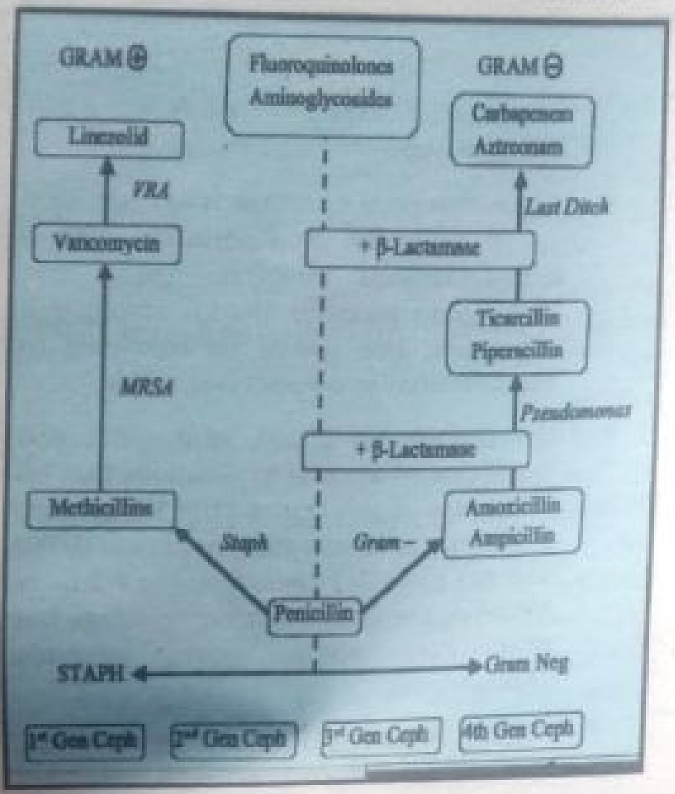
- To obtain gram negative coverage start with **Amoxicillin** or **Ampicillin** together (with or without a **beta-lactamase inhibitor**). They don't cover pseudomonas.
- If **pseudomonas coverage** is needed, step up to **Ticarcillin** or **Piperacillin** with a **Beta-Lactamase Inhibitor**. These also cover gram positives (minus staph) and anaerobes. Use should be restricted to pseudomonas to prevent resistance.
- The **Quinolones** (Cipro, levo, gatti, and moxifloxacin) are oral medications that kill a little bit of this and a little bit of that. Ciprofloxacin covers gram negatives (UTIs) and has the same bioavailability PO or IV Moxi has the gram negative coverage but also gets some gram positives (Pneumonia).
- The **Aminoglycosides** (gentamicin, amikacin) are synergistic with penicillins but almost **exclusively gram negative**. This is rarely the first choice for empiric treatment.

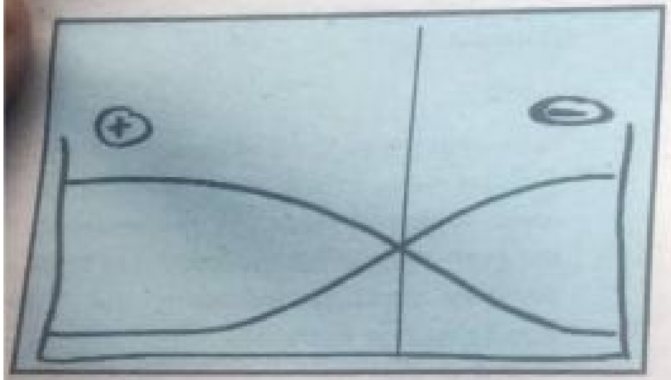
Cephalosporins

- The earlier generations of cephalosporins (the **1st Generation**) were designed to cover **strep** and **staph**. As you move up the generation ladder the amount of **gram negative coverage increases**, but the **staph coverage decreases**.
- **1st Generation Cephalosporins** are used to cover skin infections such as regular ole' cellulitis. Cefazolin.
- **3rd Generation Cephalosporins** have sufficient gram negative and positive coverage. They also cross the blood brain barrier. They're chosen first for meningitis and inpatient pneumonia.

Ceftriaxone.

- **4th Generation Cephalosporins** means only Cefepime; it kills pseudomonas. Like carbapenems, they're reserved for neutropenic fever or similarly immunosuppressed or severe conditions.


GRAM ⊕
Fluoroquinolones
Aminoglycosides
GRAM ⊖
Linezolid
Carbapenem
Aztreonam
VRA
Last Ditch
Vancomycin
+ β-Lactamase
Ticarcillin
Piperacillin
MRSA
Pseudomonas
+ β-Lactamase
Methicillins
Amoxicillin
Ampicillin
Staph
Gram –
Penicillin
STAPH
Gram Neg
1st Gen Ceph
2nd Gen Ceph
3rd Gen Ceph
4th Gen Ceph

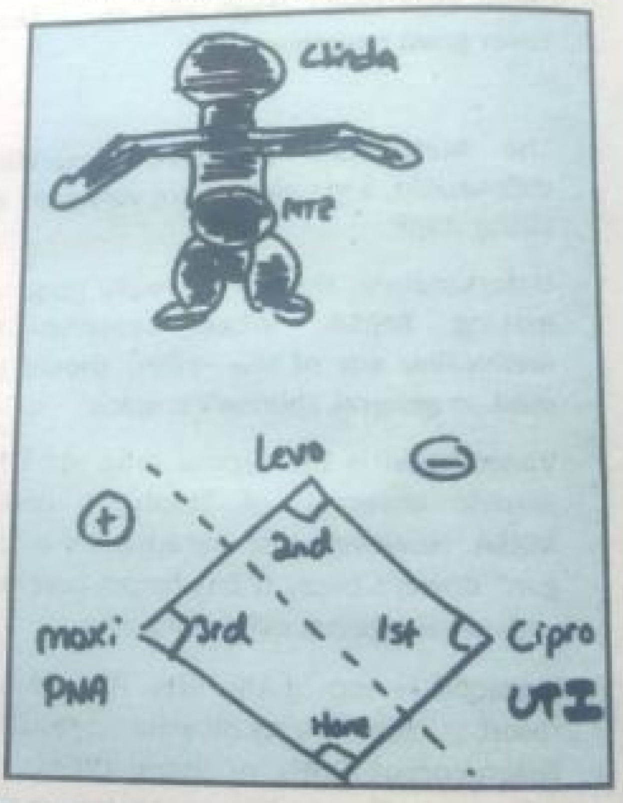


naerobes

- Anaerobic coverage comes in many forms.
- Zosyn (Pip/Tazo) has coverage, as do the penems.
- But when the focus is strictly on anaerobes there are two options: **metronidazole** (gut and vagina) and **clindamycin** (everywhere else).

Understanding Quinolones

- The more advanced the generation of quinolone, the more coverage it obtains.
- That's to say, 1st generation ciprofloxacin has gram negative coverage only; it's used to treat associated gram negative infections.
- Third generation moxifloxacin has additional gram positive coverage, but DOESN'T LOSE its gram negative application.
- This makes moxi a highly attractive medication to use (single-agent, covers everything) – but it also breeds resistance.
- Stay *away* from medications like this because they're rarely the right answer.
- No Quinolone covers Staph or Pseudomonas, though Cipro can be used in "double-coverage" of pseudomonas.


Clinda
MTZ
Levo
−
+
2nd
moxi:
PNA
3rd
1st
Cipro
UTI
Home

Pulling the trigger and going broad

- In general, the goal's to narrow the antibiotics to exactly what's being treated.
- For a staph infection, pick Nafcillin.

- For MRSA, pick Vanc. For a UTI, pick Ampicillin or Cipro.
- For pseudomonas, pick Zosyn.
- But there will be a time when a person is just ill. They're super sick and missing the bug could be fatal.
- When the person is **sick as shit** (think septic shock) it's ok to just "go broad" – make sure you get it all. This is why Vanc + Zosyn is so popular in the hospital. It's also why it will be the wrong answer on the test.
- Once **cultures and sensitivities** come back, it's then possible to narrow the antibiotics. You can also **de-escalate**, one antibiotic at a time, and assess the clinical response.

Real Life Antibiotics

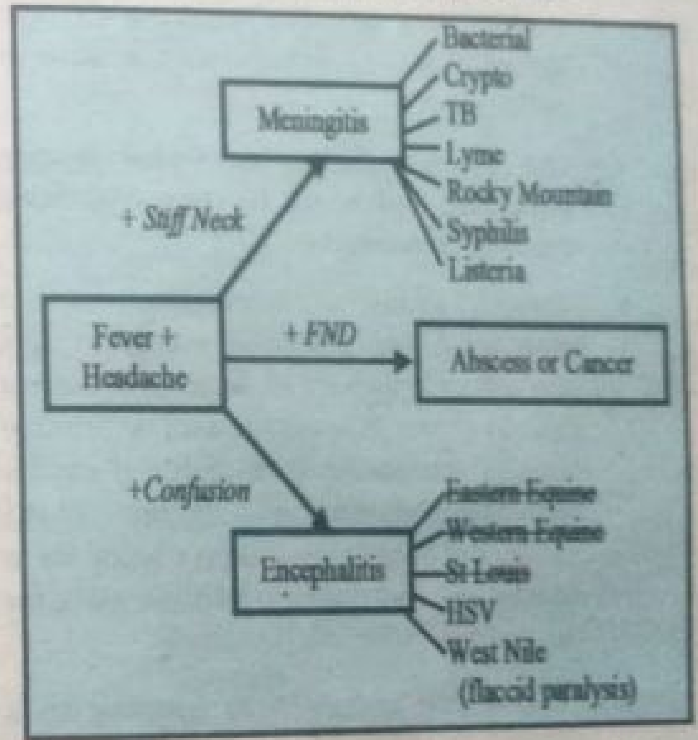
- Memorize the prevalence and patterns of infections and your institutions and use the empirically-derived-data for empiric coverage. This is the list to the right.

Condition	*Drugs*
Penicillin Allergic	Rash: Cephalosporins OK Anaphylaxis: Cephalosporins NOT ok
MRSA	Vancomycin, Linezolid, Daptomycin
Pseudomonas	Pip/Tazo (Zosyn), Carbapenems, Cefepime
Outpatient Pneumonia	Doxycycline, Azithromycin, Moxifloxacin
Inpatient Pneumonia	3rd Gen Cephalosporin + Azithromycin (CAP) Vancomycin + Zosyn (HAP)
Neutropenic Fever	4th Gen Cephalosporin (Cefepime) Carbapenems
UTI	TMP-SMX, Nitrofurantoin
Meningitis	Vanc, Ceftriaxone, +/- Steroids, +/- Ampicillin
Cellulitis	Cefazolin, Bactrim, Clindamycin IV Vancomycin

BRAIN INFLAMMATION

Presentation and Differential

- Any brain inflammation will present with a backbone of **fever + a headache**.
- This is nonspecific for a particular diagnosis, but antennae should go up for "problem in the brain."
- Other signs and symptoms that help (**photophobia**, **N/V**, and **seizures**) may be present but are likewise nonspecific.
- There are 3 categories of disease - each with their own unique findings. [1]**Meningitis** will have a **stiff neck** (Kernig and Brudzinski's Signs), [2]**Abscesses** will present with **Focal Neurological Deficits**, and [3]**Encephalitis** will present with encephalopathy (**aka confusion**).



Encephalitis

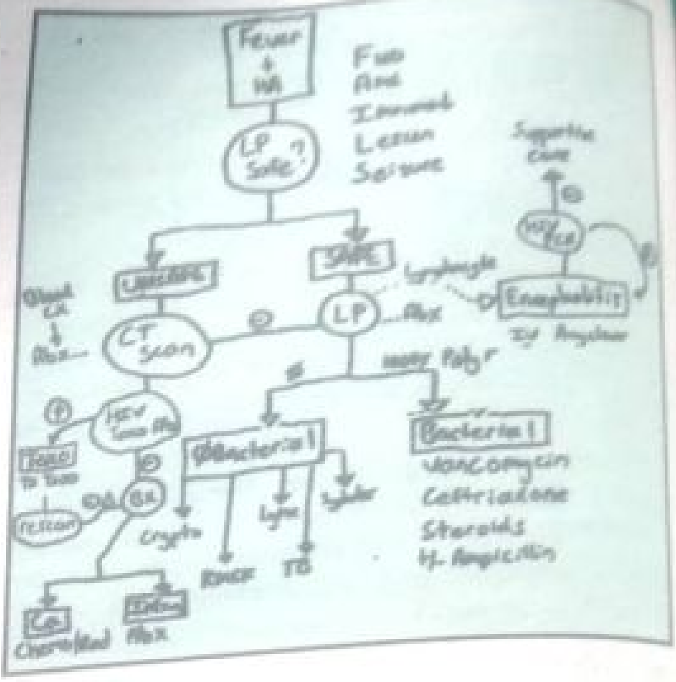
- Encephalitis is the inflammation of the brain parenchyma itself.
- It should present with the **fever + headache** AND **confusion**.
- Altered mental status is part of the FAILS mnemonic, and so a **CT is performed** before the LP.
- The CT should be normal (the test may say something about **temporal lobe** or

anosmia, implying that the question is about HSV).

- The LP should reveal a **bloody tap** (while only 30% are bloody, it's still a classic teaching).
- What separates it from a subarachnoid hemorrhage is the presence of white cells.
- Definitive diagnosis is made with **HSV PCR.**
- Treat empirically with **Acyclovir** while awaiting the results of the PCR.
- The other association to know is that west **nile virus** presents with **flaccid paralysis**.

Abscess vs Cancer (Mass Lesions)

- Since mass lesions present as a **fever** and **a headache** with **Focal Neurological Deficits**, this will also require a **CT scan** before the LP - usually with a dose of ceftriaxone.
- The CT will come back ⊕for a **ring enhancing lesion**; it'll be contraindicating the lumbar puncture.
- Instead, additional investigation of the mass must take place (i.e. a **Biopsy**). This will tell us if there's an **abscess** requiring drainage and investigation of a primary source, (**⊕organisms**) or if it's a **cancer** requiring radiation and chemo. That's useful since antibiotics won't work for a cancer, nor will chemo/radiation work for an abscess.
- There's one exception to jumping to a biopsy - an **HIV/AIDS** patient.
- In a patient with a CD4 count < 200 AND a Toxo Antibody positive at any time in life, the mass is **Toxoplasmosis 90%** of the time. For this patient **treat empirically with pyrimethamine** and **sulfadiazine** for **6 weeks**.
- If there's improvement keep it going. If not, go to biopsy.
- If "treat empirically" isn't an option, look for Toxoplasmosis-Ab.


Fever + HA
And
Lesion
Seizure
LP Safe?
UNSAFE
SAFE
Blood Cx
Abx
CT Scan
LP
Abx
Lymphocyte
Encephalitis
IV Acyclovir
HSV PCR
Supportive Care
Poly
Bacterial
Vancomycin
Ceftriaxone
Steroids
H. Ampicillin
Bacterial
Crypto
Lyme
Syphilis
TB
HIV Toxo Ab
Toxo Tx
Rescan
Bx
Ca
Chemo/Rad
Abx

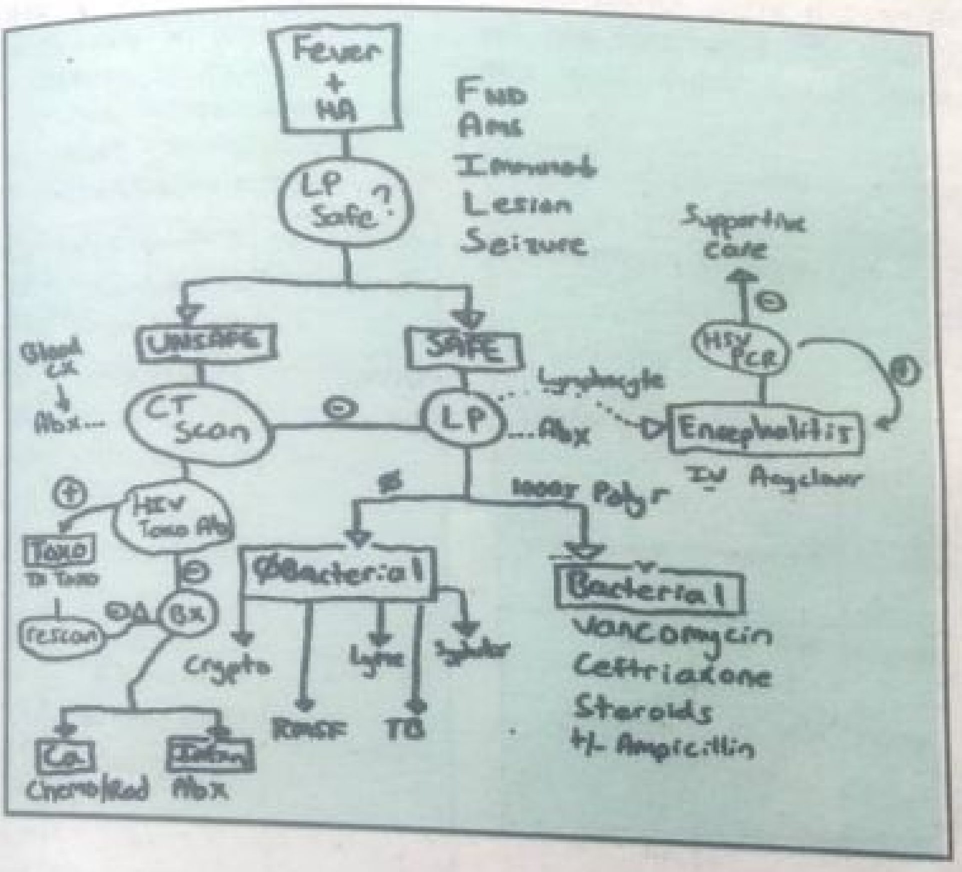
Meningitis

- Meningitis is inflammation of the meninges caused by any of etiologies. The challenge is to identify which organism is most likely, confirm it, then treat it.
- The definitive test is the **Lumbar Puncture**.
- It gives a wealth of information (glucose, protein, cells) of the CSF as well as a body fluid for **Gram Stain** and **Culture**. But sometimes you can't just jump straight to an LP. A CT must be done first if they have any of the FAILS mnemonic.
- Hence, two treatment pathways:

Bug	*Cell count*	*Glucose*	*Protein*	*WBC*	*Tx*
Bacterial	↑↑↑	↓↓	↑	PMNs	Ceftriaxone
Viral	↑	-	↑	Lymph	
Fungal	↑	↓	↑	Lymph	
TB	↑	↓	↑	Lymph	

1. The LP is UNsafe. This treatment plan uses the **blood culture** as a chance at getting a diagnosis. **Antibiotics** are given prior to the CT scan and the LP. Cultures are sterilized after 2-4 hours. Then the **CT scan** is done; if it's normal the **LP** follows.
2. The LP is Safe. This strategy uses the **CSF culture** as the chance to get a diagnosis (aka the next step is LP). **Antibiotics** are given immediately after the LP is performed.

- The LP gives a wealth of information, but most of it is useless. The only thing you care about is the **number of cells** and **what type they are** (lymphocytes or neutrophils). Ignore pH / glucose / protein for most questions.


Fever + HA
FND
AMS
Immunod
Lesion
Seizure
LP Safe?
UNSAFE
SAFE
Blood Cx
Abx...
CT Scan
⊖
LP
...Abx
Lymphocyte
Encephalitis
IV Acyclovir
HSV PCR
⊖
Supportive care
⊕
1000s Polys
HIV Toxo Ab
⊕
Toxo
Tx Toxo
⊖
rescan
⊖Δ
Bx
ØBacterial
Crypto
RMSF
Lyme
TB
Syphilis
Bacterial
Vancomycin
Ceftriaxone
Steroids
+/- Ampicillin
Ca
Chemo/Rad
Infxn
Abx

- If there are mega (100s to **thousands**) **neutrophils** you can be assured that it's a bacterial meningitis.
- Its treatment revolves around **Vancomycin, High-Dose Ceftriaxone,** and **Steroids.**
- In the immunocompromised, include **ampicillin** to cover for listeria.
- If the LP comes back "no bacterial" then we have a dilemma. It's "easy" to find what you're looking for when you know what you're seeking, but hard to find something if you don't know what it could be.
- **Cryptococcal meningitis** is found in patients with **AIDS** and **a CD4 count < 200.** There may be seizures. **Opening pressure** is often quite elevated and serial taps may be required to keep the pressure down. **Diagnose** with a **cryptococcal antigen** (do NOT use India Ink). **Treatment** is with induction for 2 weeks with IV **Liposomal Amphotericin B** and IV **Flucytosine,** followed by consolidation with PO **Fluconazole.**
- **Lyme** disease can be suspected if there's a **targetoid lesion** and travel to endemic areas such as New England. There's often NO tick noticed because they're so small.

Use **ceftriaxone** for Lyme meningitis (not doxycycline as you do for non-invasive disease). Borrelia burgdorferi is the bacteria. Ixodes is the Tick.

- **RMSF** is seen in **campers who develop a peripheral rash that moves towards the trunk. Obtain the antibody on the CSF. If positive, treat it with ceftriaxone.**
- **TB** meningitis is simply extrapulmonary TB. Consider this in someone who has Pulmonary TB risk factors. Treat with RIPE.

Bug	Suspicious Hx	Test	Tx
RMSF	Rash on hands, Spread Proximal	Antibody	Ceftriaxone
Lyme	Targetoid Rash, Hiker, Ticks	Antibody	Ceftriaxone
Crypto	HIV/AIDS	Antigen	Amphotericin
TB	Pulmonary TB	AFB	RIPE
Syphilis	STD, Palmar Rash, DCMLS	`RPR	Penicillin
Listeria	Elderly Neonate on Steroids	-	Amicillin
Viral	Diagnosis of Exclusion		

EARS NOSE THROAT

1) Otitis Media

- Otitis media is an infection of the middle ear caused by the **respiratory bugs**.
- The disease is characterized by a **unilateral ear pain** that they tug on (**relief of pain with pulling pinna)**.
- The diagnosis is confirmed by **pneumatic insufflation** (a little puff of air reveals a **tense immobile** membrane) and visualization of a moderately bulging tympanic membrane.
- While a middle ear effusion is required for diagnosis, the presence of this by itself does not diagnose acute otitis media.
- ***First line treatment*** is **amoxicillin**. If it **recurs**, use **amoxicillin-clavulanate**. If it ***re-recurs*** (3x/6 months of 4x in 12 months) ear tubes **(tympanoplasty)** are indicated. If ***penicillin allergic***, try a cephalosporin such as **cefdinir** if no anaphylactic history to penicillins, **azithromycin** if there is.

Most Common	S. Pneumoniae *H. influenzae* *M. catarrhalis*	Amoxicilin (1st line) ± clavulanate
Otitis Externa	*Pseudomonas*	Treat with topical antibiotics and topical steroids Think malignant OE
Ear Pain	Otitis Media Otitis Externa Foreign Body	Visual inspection Prinna manipulation Lidocaine / Retrieval
Rhinorrhea	Viral sinusitis Bacterial Sinusitis Foreign Body	< 10 days Treat with abx Inspection
Sore Throat	Bacterial Viral Mono	Rapid Strep → Culture Symptomatic tx Monospot
Bloody Nose	Digital Traurna	Cold compress, lean forward, ablation if recurrent

Mastoiditis

- This is a potential complication of acute otitis media where the mastoid air cells become acutely infected.
- Risk is increased with **tympanoplasty** (for pseudomonas).
- If there's acute otitis media and **swelling behind the ear** or **anteriorly rotated ear**, prompt surgical evaluation is needed.

2) Otitis Externa

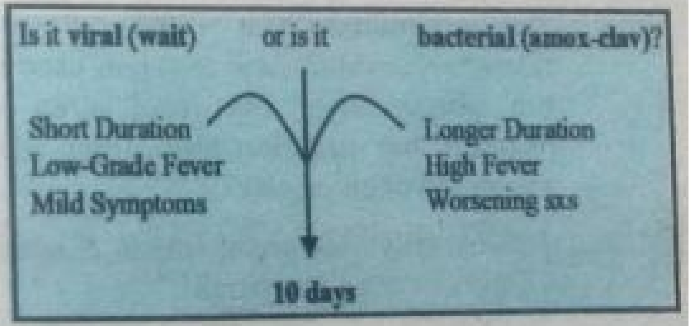
- Otitis externa presents as **unilateral ear pain** (like media), but there's **pain on palpation of pinna** (unlike media).
- Caused by frequent contact with water ("swimmer's ear"), it's commonly caused by **Pseudomonas**.
- It can also be caused by repeated trauma or an infection by **Staph aureus**.
- On physical exam an **angry erythematous canal** can be seen.
- It usually improves spontaneously.
- It becomes important to educate patients not to put anything in their ear and to dry their ears after swimming and showering.
- Treat with **topical antibiotics and topical steroids**.
- Oral antibiotic therapy is only needed if severe disease or evidence of malignant OE.

3) Sinusitis

- An infection of the **nose** and **sinuses** that occurs in both **kids and adults.**
- **Purulent nasal discharge** is a giveaway something's wrong nearby.
- **Adults and older kids** may complain of a congested, stuffed feeling with **sinus tenderness**.
- Radiographs are **not necessary** but will show **air-fluid levels** and **opacification** (XR + CT). They're expensive and are usually reserved for refractory or recurrent sinusitis to make sure there's no anatomical defect.
- But before doing anything make sure this isn't just a cold - a regular viral illness.
- If it's been > **10 days** simply **presume bacterial infection**.
- In patients with severe symptoms (high fever > 39°C, purulent nasal discharge/facial pain for 3-4 days) or **acutely worsening** symptoms (especially after initial improvement) then antibiotic therapy should be considered.
- This is an URI so treat the URI bugs with **amoxicillin-clavulonate**.
- ***Don't use azithromycin! In younger children with symptoms of sinusitis, don't forget to evaluate for a foreign body.***

4) Cold – Viral Nasal

- Typically caused by **rhinovirus** and transmitted between people by **large droplets**.
- It's also gives "boogers", **rhinorrhea**, **congestion**, and **low-grade fever** so it looks like sinusitis.
- **Don't perform any studies** – this includes nasopharyngeal washes, cultures, PCR, imaging, etc.
- If it's **<10 days** it's likely viral - the patient should wait it out.



5) Pharyngitis

- Much like sinusitis, **viral** pathogens are the most common cause occurring in kids and adults.
- The primary complaint will be **sore throa** with **pain on swallowing**.

- Some exam findings (pharyngitis plus conjunctivitis = adenovirus; pharyngitis plus rash on palms/soles = coxsackie) can help point towards a specific pathogen. Because a bacterial infection with **Group A Strep (GAS)** can cause **rheumatic fever, if untreated, diagnosing and treating this is important.**
- **Post-strep glomerulonephritis** (PSGN) **can still happen even if you get treated for Strep A Pharyngitis.** The symptoms are the same whether it's viral or bacterial; the job becoming deciding whether to treat empirically, or if testing is needed first.
- There are **scoring systems** *(Centor,* **Modified Centor)** which can indicate the next step for the patient – supportive care, test for **GAS**, or treat for GAS*.
- Patients **under 3 years old** have the lowest incidence and **should not be tested**; ages **5-15 years** have the highest incidence so jumping straight to testing in a patient without viral symptoms (cough, rhinorrhea) is reasonable. The ***Modified Centor (aka "McIsaac") criteria*** attempt to take the higher incidence of the younger age into consideration.
- The **Rapid-Strep** test (the screening test) is **specific** (which is the opposite of how a screening test should be). This is because of the rapid turn around time (minutes). ***If positive, treat.***
- **The confirmatory test** – the culture - takes days to return, and so is only used in the setting when the rapid strep is negative, but suspicion high. Treat with amoxicillin or **amox-clav.**
- If pharyngitis + enlarged spleen is seen, it's mono. Get an EBV panel.

6) Foreign Bodies

- Kids like to stick things in places. Things can go into the **nose** (producing **foul-smelling unilateral** rhinorrhea), **ear** (pain), and sometimes down their **throat** (aspiration).
- Essentially, the object has to be **retrieved** after seeing it and any **infection treated.**
- One particular foreign body are **insects**; homeless are aware of this and sometimes sleep with coins in their ears.
- Bugs present with a **unilateral scratching** or **buzzing** and should be treated with **lidocaine** and retrieval but **never light** (they just burrow deeper).

7) Epistaxis

- Whether out of habit or because the nose itches, epistaxis is most commonly caused by **digital trauma** (*nose-picking*).
- Normal nosebleeds are **unilateral** and last **< 30 minutes.**
- Applying a cold compress (vasoconstriction) and leaning **forward** (backwards is just drinking the blood causing a cough breaking the clot) can cause an active bleed to stop.
- Look inside the nose to make sure there isn't anything **anatomical** or **foreign** within.
- Recurrent bleeds with visible target vessel with evidence of bleeding can be **cauterized with silver nitrate** *if anterior.*
- Posterior bleeds need ENT intervention and can involve packing and empiric antibiotics.

Modified Centor (aka "McIsaac") Criteria

C	Absent Cough	+1
E	Exudates (tonsillar)	+1
N	Nodes = Anterior Chain Lymphadenopathy	+1
T	Temp > 38°C +1	+1
OR	< 14 yrs old **or**	+1
	> 44 yrs	-1

Score Interpretation

≤1	No further testing needed
2-3	Perform rapid testing
≥4	Empiric antibiotics*

Group A Strep Pharyngitis Summary

- Don't test patients with viral symptoms
- Avoid the Centor Criteria in patients under 15
- Test all patients before treating!
- Rapid test has high specificity so confirm negatives

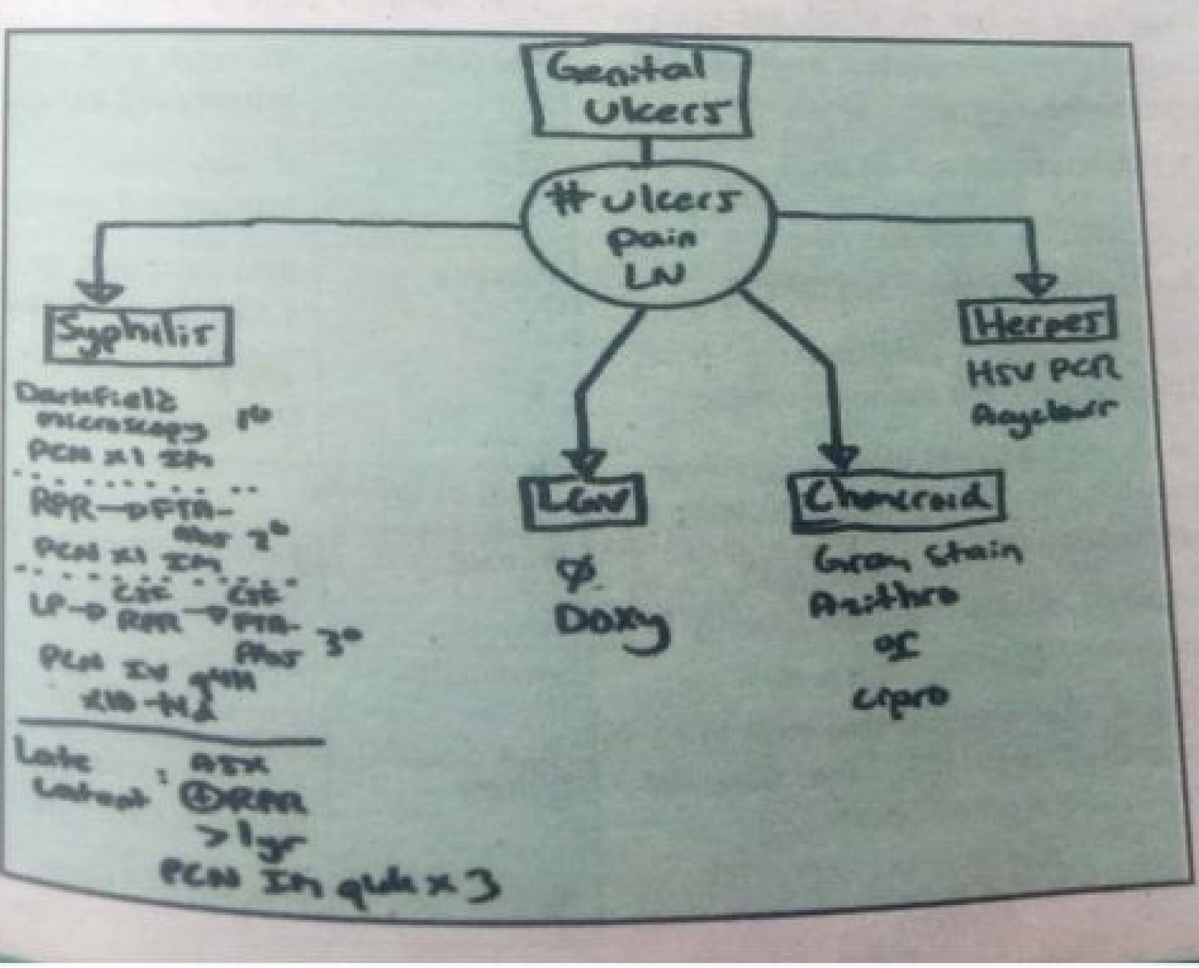
8) Choanal Atresia

- Finally, something isolated to pediatrics.
- This is an **atretic** or **anatomically stenosed** connection between the nose and mouth.
- It can be unilateral or bilateral (which is an emergency).
- In severe cases the baby will be **blue at rest** as they are obligate nose breathers (think breathing and breastfeeding simultaneously).
- They will **pink up with crying** (as he/she uses his/her mouth).
- If there's a partial obstruction there might be a **childhood snore**.
- Kids shouldn't snore.
- If there's complete atresia a **catheter will fail to pass**.
- If it's incomplete a **fiber-optic scope** will identify the lesion.
- **Surgery** is required to open the atretic passage.

GENITAL ULCERS

Intro

- Genital ulcers can be easily separated from one another based on the number of ulcers, the presence of pain, and the presence of affected lymph nodes.
- Getting to the right answer should be easy; knowing the details of each disease becomes harder (as does keeping them straight).
- **Give lots of attention to syphilis** as the others are often distractors against it.


Genital Ulcers
# ulcers
pain
LN
Syphilis
Darkfield microscopy 1°
PCN x1 IM
RPR → FTA-Abs 2°
PCN x1 IM
CSF CSF
LP → RPR → FTA-Abs 3°
PCN IV q4h x10-14d
Late Latent: ASX
⊕RPR
>1yr
PCN IM qwk x3
LGV
∅
Doxy
Chancroid
Gram stain
Azithro
or
cipro
Herpes
HSV PCR
Acyclovir

1) Syphilis

Primary Syphilis

- **Primary Syphilis** presents as a **painless ulcer** called a **chancre**.
- It represents the entry point of the **Treponema Pallidum** organism, a **spirochete**.
- There may be associated painless **lymphadenopathy**.
- It's too early to use serology so we have to look for the organisms themselves with a **Dark-field Microscopy**. At this point *IM* **PenG** will be curative.
- If the patient is ***penicillin* allergic**, **doxycycline** can be used instead.

Secondary syphilis

- **Secondary *syphilis*** is a disseminated ***targetoid*** or ***maculopapular* rash** that *involves the palms and soles*.
- *The rash is* ***infectious***.
- By this time serology is positive.
- *Screen for* syphilis with a non-treponemal test such as ***RPR*** (or VDRL) and confirm with a treponemal test such as ***FTA-Antibodies***.
- *If FTA-Abs⊕ treat with IM PenG.*

Tertiary syphilis

- ***Tertiary syphilis*** penetrates the CSF.
- *Look for the* **Argyll-Robertson** pupil, **Tabes Dorsalis**, and any neuro symptom.
- *Do serology, only this time the "serology" should be on the CSF fluid following a* ***lumbar puncture***.
- *In tertiary syphilis the patient needs* ***IV Penicillin x 7-14 days***.
- *If allergic AND pregnant they have to be* ***desensitized*** *and given the penicillin anyway; doxy is contraindicated.*

latent syphilis

- If the patient has a **positive RPR** but no symptoms, it's said to be **latent syphilis**.
- If it's within one year of contraction, it's early **latent** syphilis and is treated as secondary.
- If the time is ***unknown or it's > 1 year*** from contraction, it's considered late **latent syphilis** and is treated with **PenG IM qWeek x 3 weeks**.

TESTS FOR SYPHILIS

RRR	Good **sensitivity** requires > 1 month to be positive
VDRL	Decent sensitivity, False ⊖ with Lupus
FATA-abs	Good specificity, confirmatory for PRP ⊕
Darkfield Microscopy	Excellent **specificity,** only means of diagnosis for **primary** **chancre**, can be used on 2o lesions
Treatment for Syphilis	
Pen G IM	Mainstay of therapy, x1 time **primary** and **secondary**
Doxy	If **Pen Allergic** x7 days for **primary** and **secondary**
Pen V IV	Best treatment for **3o disease** x 14 days, or for **penicillin** **allergic pregnant patients** (desensitize)
Types of Syphilis	
Primary	**Painless chancre** with **Inguinal Lymphadenopathy**
Secondary	Maculopapular **Rash** on **hands** and **soles** (infectious)
Teritary	Any **neurologic** complaint (Argyll-Robertson Pupil)
Early	Positive RPR and

Latent	< 1 year from contraction
Late Latent	Asymptomatic Positive RPRP and > 1 year from contraction, or unknown

Dx	Presentation	Test	Treatment
Syphilis	Painless but firm ulcer (**singular**) + Lymphadenopathy	1°=**Dark Field** 2° **RPR → Abs** 3° **LP** of 2°	**PenG IM** or **Doxy** **PenG IM** or **Doxy** **Pen IV x 14 days**
Ducreyi	**Painful (singular)** + Lymphadenopathy	Gram Stain + **Culture**	Azithromycin or Ciprofloxacin
Herpes	**Roofed vesicle** on an **erythematous** **base** after a **painful** **prodrome**	HSV PCR	**Acyclovir** Valacyclovir
LGV	Painless singular ulcer, Pussy LN	needed	**Doxy**

Hemophilus ducreyi

- You "**do cry with ducreyi**" presenting as a syphilitic chancroid **that hurts.**
- It will have the ulcer, erythematous base, and inguinal lymphadenopathy of syphilis, but this **will hurt** - syphilis doesn't.
- Do a simple **gram stain** and **culture**, then treat with antibiotics. **Azithromycin** or **Cipro** will do the job.

Herpes

- **Herpes Hurts** like ducreyi, but are often **multiple roofed vesicles**, each on an **erythematous base**, whose eruption is preceded by a **painful prodrome.**
- If this classic picture is seen just treat with **acyclovir** as the diagnosis is clinical.
- At times, however, vesicles can **unroof** and become **confluent.**
- This makes clinical diagnosis difficult.
- Diagnose definitively with an **HSV PCR.**
- The Tzanck prep is no longer recommended given the absence of specificity and sensitivity.

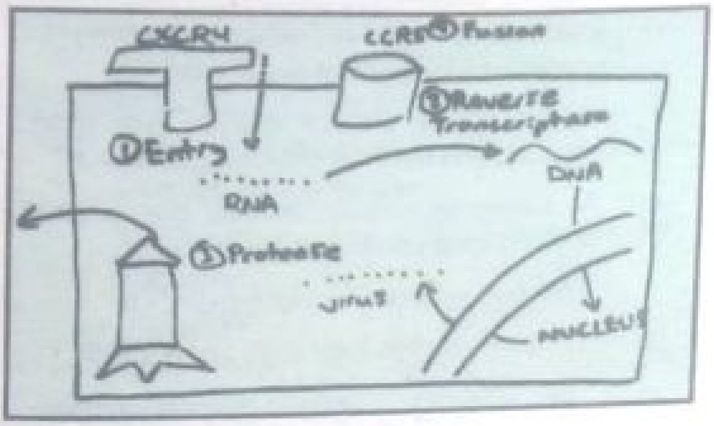
4) Lymphogranuloma Venereum

- It is caused by C. trachomatis. It presents as a **painless singular ulcer** (much like Syphilis), but has **painful lymphadenopathy** that's often **supportive** (pus).
- While a nucleic acid amplification assay will confirm the diagnosis, treatment is often supportive or with simple antibiotics such as **doxycycline.**

HIV

Pathology and Diagnosis

- HIV is a **Retrovirus** that enters **CD4 cells** via **gp120** and **gp41** (CCR5, CXCR4 chemokine receptor bearing cells).
- Once infected, reverse transcriptase turns the RNA virus into host DNA, hijacking the nucleus to produce HIV RNA.
- After replication, new virions are packaged by **proteases** and are released into the blood stream by **exocytosis.**
- CD8 responses cause death/loss of CD4 cells resulting in a major decline.
- **Diagnosis** is based on **ELISA** confirmed with **Western Blot** or **Viral Load.**
- During the window period (~6 weeks from infection to antibodies) only viral load can be used to make the diagnosis.
- This is useful in **acute retroviral syndrome.**



Opportunistic Infection Prophylaxis

- As the **CD4 count falls** the patient becomes vulnerable to **opportunistic infections.** We look for these opportunistic diseases and treat them.
- However, we can also **prophylaxis** against three diseases:
  1. **PCP pneumonia** at a **CD4 <200** with **TMPSMX.**
  2. **Toxo** at a CD4 < 100 with **TMP-SMX** and
  3. **MAC** at a **CD<50** with **Azithromycin.**
  4. If you can't use TMP-SMX, use **Dapsone.**
  5. If G6PD deficient, use **Atovaquone.** TMP-SMX = Bactrim.

Opportunistic Infections and Therapy

- In spite of limited prophylaxis many patients do get infected with opportunistic infections. Knowing what to look for and what to treat based on CD4 count is critical.
- Be aggressive in the treatment of opportunistic infections.
- It comes down to simple memorization (the chart to the right) and recognition of symptoms.
- Note that **AIDS** is defined by a **CD4<200** OR **Opportunistic Infection.**
- Since it can't currently be cured the patient will always have the label - even if the infection clears or CD4 counts rise to normal levels.
- HIV is a blood borne illness and a sexually transmitted disease.
- Be sure to **screen** for **possible coinfections** at high risk.
- It's the infections seen with the same risky behavior (IVDA and sex) such as **cervical cancer, Hep B** and **Hep C, Syphilis,** and GC/Chlamydia.

Antiviral Therapy = HAART

- Start HAART as soon as HIV is diagnosed.
- Typical therapy involves the 2+1 **approach.**
- That means 2 **Nucleoside Reverse Transcriptase Inhibitors** and 1 Other thing.
- The "other thing" could be a **Protease Inhibitor** (boosted with ritonavir), a **Non-Nucleoside Reverse transcriptase inhibitor,** an **Integrase Inhibitor,** or **Fusion Inhibitor.**
- You choose which drug to use based on the patient's preference and the **genotyping** (the closest to a culture we have).
- If a patient gets on HAART, stays on HAART, and never misses a dose they can lead essentially normal lives.

Prophylaxis to HIV

- Both **Pre-Exposure prophylaxis (PrEP)** and **Post-Exposure Prophylaxis** (PEP) are highly effective at reducing HIV transmission.
- **Tenofovir + Emtricitabine** is typically used.
- Vertical transmission can be prevented with **AZT** when used **at the time of delivery** (and also by treating mom during pregnancy).

CD4 Count and Viral Load

CD4	What's Right Now = Infection Risk
Viral Load	What's to come = CD4 change

CD 4	*Vulnerability*	*Prophylaxis*
>350	Ø	Ø
>200	Thrush, TB, Leukoplakia	Ø
<200	PCP Pneumonia	1st Bactrim 2nd Dapsone 3rd Atovaquone
<100	Toxo	1st Bactrim 2nd Pyrimethamine
<50	MAC	Azithromycin

Count	*Infection*	*Treatment*
>500	Normal person with normal infections	Normal
200-500	Oral Leukoplakia Pulmonary TB (>5mm) Pneumococcal PNA Thrush	INH (Latent), R.I.P.E (Active) 3rd Gen Ceph + Macrolide Nystatin S+S
<200	PCP Pneumonia Crypto Meningitis Esophageal Candidiasis	Bactrim, Dapsone Amphotericin + Flucytosine Fluconazole
<100	HSV/CMV Esophagitis Toxoplasmosis	Acyclovir/Ganciclovir Pyrimethamine Sulfadoxine
<50	Disseminated MAC CMV Retinitis	Clarithromycin + Ethambutol Valaciclovir, Foscarnet

INFECTIVE ENDOCARDITIS

Pathogenesis

- Infective Endocarditis (IE) is an infection on the heart valves.
- To get infected there must be introduction of bacteria into the blood stream AND a bad valve.
- Thus, some risk factors are **intravenous drug use** (most common in the US) or a patient with repeated access (like dialysis).
- Others are **valvular damage** (rheumatic heart worldwide, congenital defects in the US) and a **history of endocarditis** (100 fold increase in risk).
- Once the infection sets up shop on the valve, embolic, vascular and rheumatologic manifestations are possible.

Major Criteria
Sustained Bacteremia **by organism known to cause IE** *(Strep, Staph, HACEK)*
Endocardial Evidence by Echo
New valvular regurgitation *(increase or change of pre-existing not adequate)*
Minor Criteria
Predisposing Risk Factor (valve disease or IVDA)
Fever ≥ 38 C
Vascular Phenomena *(septic emboli arterial, pulmonary, and Janeway lesions)*
Immunologic Phenomena *(glomerulonephritis, Osler nodes, Roth spots, RF)*

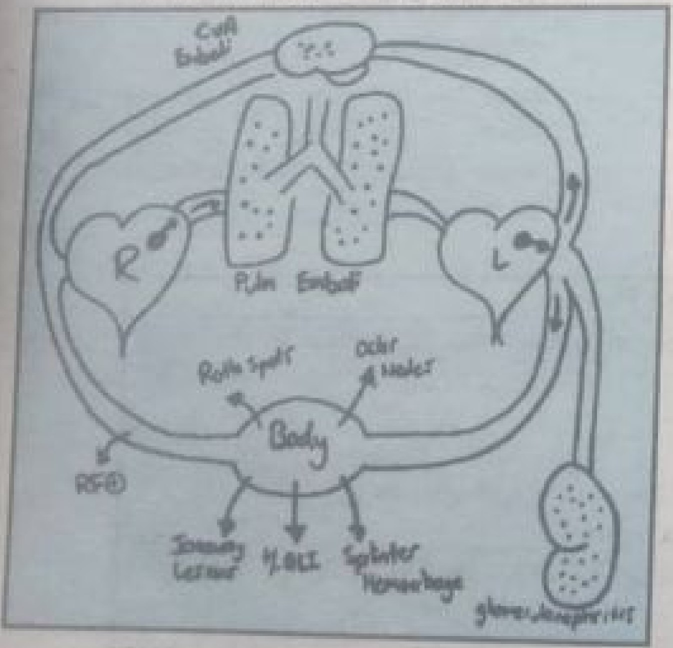
Definite
Two major criteria (Blood Culture and Echo)
One major and 3 minor
5 minor
Possible
1 major and 1 minor (almost every bacteremic patient, btw)
3 minor
Rejected
Firm alternative diagnosis explaining evidence for IE
Resolution of everything in 4 days
No pathologic evidence (a BIOPSY!?) at surgery or death
Failure to meet criteria as above

Presentation

- The Duke's criteria (presented to the right) is a useful means of building a table you can memorize.
- However, it was created for study inclusion and isn't a diagnostic tool. Instead, note there are two types of endocarditis: **Acute and Subacute.**

Acute Endocarditis

- **Acute Endocarditis** is going to be from virulent organisms (Staph, Strep Pneumo) that will infect normal, native valves.



- These patients will be sick: persistent bacteremia, valve destruction, **new murmur**; we order a bunch of cultures to watch it clear (or not) and start antibiotics right away.
- Since the presentation is obvious, it doesn't take long for the patient to seek medical attention.
- Thus, there's no time for the rheumatologic manifestations to start.

Diagnostic Steps

Blood cultures x 3, one hour apart, NO abx	Subacute Endocarditis
Blood cultures x 2 now, start empiric abx, followup cultures	Acute Endocarditis
Trans Thoracic Echo	If you aren't sure
Trans Esophageal Echo	If you are sure

Subacute Endocarditis

- **Subacute Endocarditis** is caused by less virulent organisms (S. bovis, S. viridans, HACEK) infecting abnormal native valves.
- It's the endocarditis people learn about in second year – **Roth Spots** (eyes), **Janeway lesions** (painless hands), **Splinter Hemorrhages** (nail beds), **Osler nodes** (painful distal digit pulp) etc - subtle clues pointing to endocarditis because the patient isn't sick enough to warrant attention.
- This one requires multiple cultures to make a diagnosis; antibiotics shouldn't be started right away.

Diagnosis

- The **echocardiogram** and **blood cultures** are the cornerstone of diagnosis.
- The TTE is often used first (usually to identify a valvular abnormality rather than a vegetation) followed by a **Transesophageal Echocardiogram** to make the final diagnosis by identifying the vegetation. The TEE is the best test.
- **Acute endocarditis**: hey, the bacteremia won't clear. Keep getting cultures until they do. ***OH NOES! A MURMUR! Get a TEE.***
- **Subacute endocarditis**: my my, look at these interesting rashes. This one is painless on their hands, their nail beds have these small splinter like splotches, and their RF is up. I wonder if this is rheumatoid arthritis? Doesn't sound like RA - get a culture…no… get THREE cultures… and wait. AHA! BACTEREMIA! GET A TEE!!!!!!

Treatment

- There are ***two elements*** to the treatment of Endocarditis: **antibiotics** and **surgery**.
- Antibiotics will be required for a **minimum of 6 weeks**. Which antibiotic is chosen will be dependent on the culture and sensitivity of the organism. But when treatment is begun we must use **empiric coverage**. That changes not on the endocarditis, but on the patient.

Antibiotics: Native Valve

All Native	Vancomycin		
Prosthetic Valve			
<60 Days	Vancomycin	Gentamycin	Cefepime
60-365 days	Vancomycin	Gentamcyin	
>365 days	Vancomycin	Gentamcyin	Ceftriaxone
SBE		Gentamcyin	Ceftriaxone

See the "vanc+gent" backbone. Just remember which ones gets Cefepime, Which one gets Ceftriaxone, and then Native valves need only Vanc

Vancomycin → Daptomycin → ~~Linezolid~~ (not for bacteremia)

Surgery

Go to surgery if
>15mm even without embolization
>10 mm + embolization
Abscess
Valve destruction or CHF
Fungus

- Surgery is designed to prevent CHF and embolization.
- Acute endocarditis can cause valvular insufficiency.
- The worse the valve or the worse the CHF the sooner the surgery (someone in cardiogenic shock goes right away while someone who is compensated but has severe insufficiency can wait a few days).
- This is a clinical judgment: how sick the patient is.
- But embolization isn't clinical. There are fairly well described criteria for who goes to surgery for a vegetation that could embolize. Note that a stroke or ***MI would be a contraindication to any surgery EXCEPT for IE,*** since failing to go to surgery will result in further embolization. See to the right.

Prophylaxis

- There's a **long** list of people that need to be prophylaxed against IE. But if you instead remember, "bad valve" and "mouth and throat" you'll get it right most of the time.
- **Bad Valve** means they have a congenital heart defect, previous endocarditis, or a prosthetic valve.

- **Mouth and throat** means they're having a dental procedure or a procedure that would involve bronchoscopy and biopsy of the respiratory flora.
- If both are seen, give **amoxicillin**. *If they can't tolerate a penicillin, use ceftaz. If that doesn't work go to clinda, but you won't be drilling down to this level of detail as a medical student.*
- Unique Associations for Bonus Points **Strep bovis** comes from the colon. If Strep bovi endocarditis, do **colonoscopy** for occult cancer.
- **Staph aureus** comes from the skin. IVDA and tricuspid valve most often.
- **Strep Anything Else** comes from the mouth. Look for dental disease.

Bad Valve	**Mouth and Throat**
Congenital Heart Disease	Dental Procedures
Prosthetic Valve	Biopsy of the Airway
History of Endocarditis	

↓

Antibiotics

Amoxicillin (1st line)

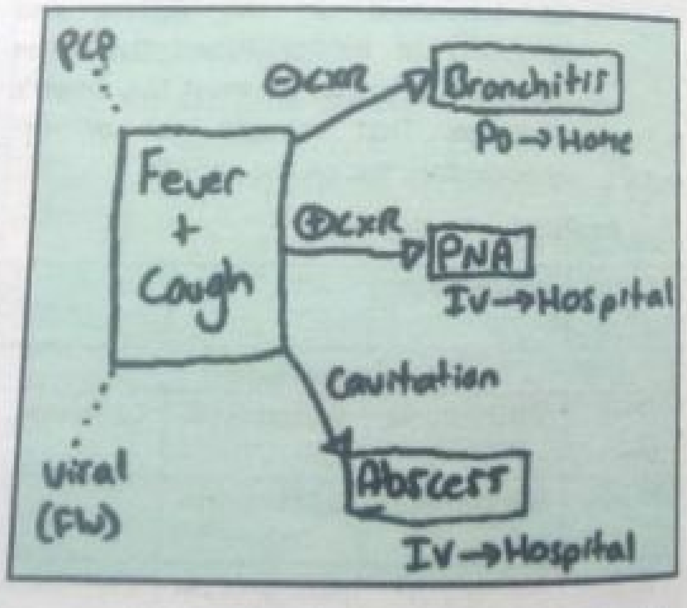
Ceftaz (back up)

Clinda (last line)

PNEUMONIA

Organisms and Disease Typing

- Whenever there's a **fever and a cough** consider a lung infection.
- There are three lung infections: 1) **Abscess**, 2) **Bronchitis**, and 3) **Pneumonia**.
- When learning about **Typical Pneumonias** and **Atypical Pneumonias**, the symptoms and CXR findings may be misleading (neither is specific enough), and "Pneumonia" is treated on its severity - not by which "type" it is.
- Instead, use: exposure, the history, and risk factors to orient the treatment goals.
- Rather, the thinking should be along the lines of, "given the patient's risk factors, what bug could this be?"
- If there's **no association with healthcare** the community bugs (not virulent or resistant) are more likely (**Community Acquired Pneumonia**).
- Within CAP there are bugs more likely to cause disease. **Strep pneumo** is always the most common; the #2 disease is based on risk factors.
- If the patient has been **near healthcare** the virulence and resistance increase; the bugs are more hostile.
- Treat for HCAP (**Health Care Associated Pneumonia**).
- To be considered HCAP (which also means HAP and VAP), there must be exposure to a healthcare facility **within 90 days** (HCAP), be admitted and acquire the pneumonia **after 48 hours of admission** (HAP), or be on a **ventilator** (VAP).
- While HCAP, HAP, and VAP are different bureaucratically, they carry the same microbiologic risk - MRSA and Pseudomonas – so they're treated the same.



- If the patient is **Immunocompromised** the weird bugs can cause infections (TB, Fungus, MAC, and **PCP**).

- Finally, if there's a risk for **aspiration** (MS, Stroke, Diabetic, Alcoholic, Intubated, Seizures), the oral flora /anaerobes are at ↑ risk.

orkup

- Everybody who presents with a **fever** and a **cough** will get a **CXR**.
- They'll also get an **SpO2**. Even though the best test is a culture, sometimes in the lung it doesn't work out. So beyond CXR + SpO2, there's no clear algorithm.
- Sputum Gram Stain and Culture rarely has utility unless obtained by bronchoscopy (contaminated by floral organisms, useful only when <10 Squamous and >25 Polys /hpf).
- **Blood Cultures** rarely yield anything, and if positive represent septicemia, but should be obtained on any patient being admitted to the hospital.
- **Bronchoalveolar lavage** is reserved for acutely ill patients or those who do not improve after 72 hours of empiric therapy.
- **Serum, urine antigen,** or **PCR** can be used to identify certain organisms (legionella, strep pneumo), but these advanced tests are often not needed.
- **Empiric treatment** is usually sufficient to direct us.

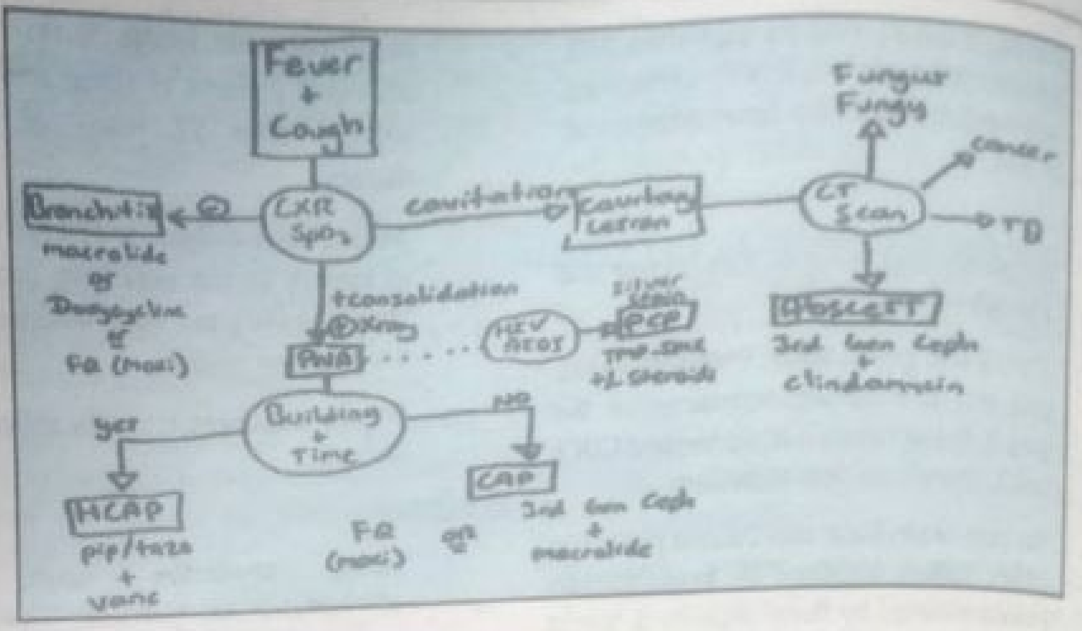
Pneumonia

- **Fever, productive cough,** and **consolidation on chest x-ray** is classic for pneumonia.
- In this constellation, one must only decide between HCAP and CAP; use empiric therapy from there.
- Be able to differentiate Pneumonia from Abscess and Bronchitis, as well as HCAP from CAP.

CAP	Strep pneumo	Most Common
	M. catarrhalis	
	H. flu	COPD / Smoker
	Klebsiella and Anaerobes	Aspiration (EtOH, CVA, MS)
	S. Aureus	Post Viral
	Legionella	Immuno ↓
HAP	Pseudomonas	
	MRSA	
Immuno ↓	TB	
	Fungal	
	PCP	

Fever + Cough…….with

Bronchitis	Sputum Production, Nrml CXR
Abscess	Foul Breath, Cavitation CXR
Pneumonia	Sputum production, Consolidation on CXR
PCP	Immunocompromised, Hypoxemia, elevated LDH
Flu	Myalgias, Arthralgias, body aches


Fever + Cough
CXR Sp?
Bronchitis
⊖
macrolide or Doxycycline or FQ (moxi)
cavitation
Cavitary Lesion
CT Scan
Fungus Fungy
cancer
TB
Abscess
3rd Gen Ceph + clindamycin
+consolidation ⊕Xray
PNA
HIV AIDS
silver stain
PCP
TMP-SMX +/- Steroids
Building + Time
yes
no
HCAP
pip/tazo + vanc
CAP
3rd Gen Ceph + macrolide
FQ (moxi)
or

Bronchitis

- Bronchitis presents as a **fever** and **a cough** with a **Normal CXR**.
- This presentation might be a viral pneumonia or an extrapulmonary process, but with a **sputum production** that can be treated as an ambulatory pneumonia.
- This means outpatient therapy with a macrolide (Azithromycin), doxycycline, or moxifloxacin.
- Chronic Bronchitis is a productive cough for 2-3 months in 2 consecutive years.

S. Pneumonise	Most Common
Legionella	GI + CNS Sxs Urine Ag
Klebsiella	EtOH
Chalmydia	Placenta/Sheep Serum Ab
Haemophilus	COPD/Smoker

Bottom Line	*1st Line*	*Alternate*
Ambulatory Pneumonia ("Bronchitis")	Azithromycin	Doxycycline Moxifloxacin
Inpatient Community Pneumonia ("CAP")	Ceftriaxone + Azithromycin	Moxifloxacin
Inpatient Health Care Pneumonia ("HCAP")	Vancomycin + Pip/Tazo	Many
PCP	Bactrim +/- Steroids	None
Influenza	Oseltamivir	None

Atypical Pneumonia

- This isn't a thing in clinical medicine, but it still comes up on tests.
- Atypical pneumonia presents as an **insidious onset fever** and **cough** with **bilateral infiltrates** on CXR.
- These patients typically don't present as acutely ill - the so called "walking pneumonia."
- Treat this like a bronchitis, but know the association between **Mycoplasma Pneumonia** and IgM cold agglutinin disease.

Abscess / Aspiration Pneumonia

- An abscess is going to present as a **fever** and a **cough**, plus **cavitation** and **foul breath**. Because of cavitation, lung cancer, TB, and fungus must be considered.

- Obtain a CT scan to facilitate.
- **Clindamycin** is crucial to the therapy because oral flora has anaerobes, but often additional therapy is initiated with the clindamycin as it still represents "a pneumonia."
- Aspiration causes abscesses.
- Aspiration risk essentially means patients with **seizure**, **alcoholics**, and **MS/CVA** patients with dysphagia (include PEG tube patients in here too).

HIV and PCP

- If the patient has a subacute pneumonia with bilateral fluffy infiltrates, give consideration to PCP.
- An elevated LDH is often associated with PCP.
- The diagnosis is made with a **silver stain** on induced sputum or bronchoalveolar lavage.
- The treatment is with **IV Bactrim.**
- If the patient is **hypoxemic**, **add steroids.**

Who Needs to be admitted? PORT Score / PSI and CURB-65

- You shouldn't memorize the Pneumonia Severity Index (PSI) nor the CURB-65, but since pneumonia is so common at least be aware of what these are and what they mean.
- The **CURB-65** is an **ED Triage Tool,** whereby the patient likely needs admission if any one of the CURB-65 are met.
- The **PSI** is an **Internal Medicine Triage Tool** that's quite complex – it requires an online calculator to complete. The higher the score, the more likely the need for ICU. The lower the score the more likely the person can be discharged.
- While **clinical acumen is equivalent to these scores,** they provide object evidence for documentation and can be used to gauge clinical reasoning on severity of disease. THIS IS NOT FOR THE SHELF.

CURB-65

Confusion of New Onset Urea > 7 (BUN > 19) Respiratory Rate > 30 Blood pressure < 90 / < 60 65 years or older	A 5-point system. The *more points, the more severe the patient's condition + and the more fatal it is. Used to determine if the patient needs to be admitted*

Pneumonia Severity Index

I		Discharge from ED
II	<70	Floor Admission (probably)
III	71-90	Floor Admission (Definitely)
IV	91-30	ICU Admission (Probably)
V	>130	ICU Admission (Definitely)

SEPSIS

Introduction

- An infection usually causes a local inflammatory response with symptoms.
- Lung infections cause a cough, while UTIs cause dysuria. But when an infection jumps the shark and goes systemic - **effects are felt systemically** - start thinking of sepsis.
- Sepsis itself doesn't require **septicemia** (bacteria in the blood) and therefore may be **culture negative**, but the systemic effects of **inflammatory mediators** can wreak havoc on the body.

SIRS Criteria

- The Systemic Inflammatory Response Syndrome (SIRS) must meet **2 of 4 criteria** that signal physiologic responses to inflammation.

- Inflammatory mediators will cause ↑ CO (↑ **HR**) either directly on the heart or reflexively from vasodilation.
- **Tachypnea** follows.
- **Fever** is a product of ***IL-6 + TNF-α.*** Finally, the response to infection is ↑ **WBC** (leukocytosis). But, because some infections may ↓ WBC or a person can have sepsis in the presence of HIV, both count.
- Evaluation beyond sepsis involves looking for **end organ damage:**

  1) **Renal Failure** (↑ Cr and BUN)

  2) **liver** failure with coags and an LFT

  3) **Blood Vessels** with a blood pressure,

  4) **Brain** with mental status checks, and

  5) **Heart** with an ECG or Troponins.

  Still further, one needs to evaluate for tissue hypoxemia with a **lactic acid level.**
- Depending on the number and severity of organ dysfunction, the patient is stratified into a sepsis "type." (SIRS, Sepsis, Severe Sepsis, Septic Shock, MODS).

SIRS Criteria

Temperature	> 38 or < 36
Tachycardia	>90
Respiratory	RR > 20 or PCO_2 < 32
WBC	>12 or <4

SIRS "Types"

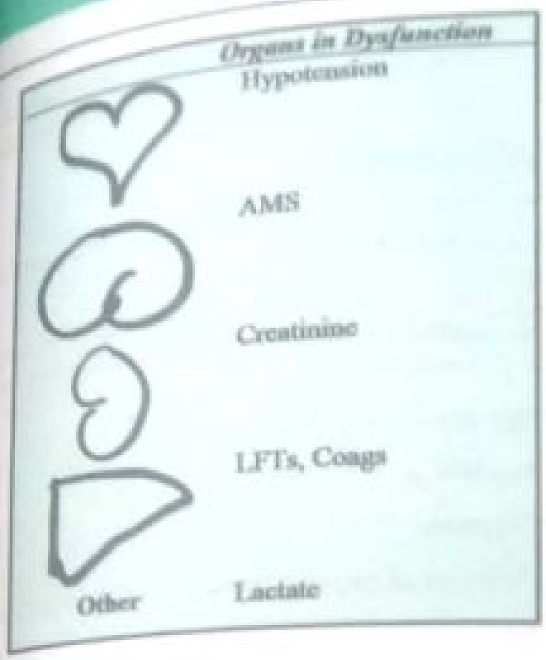
SIRS	2 or more criteria met, source
Sepsis	SIRS ⊕ source
Severe Sepsis	Sepsis with low blood pressure or elevated lactic that is **responsive** to fluids
Septic Shock	Sepsis with low blood pressure or elevated lactate that is **non-responsive** to fluid.
MODS	Multiple Organ Dysfunction Syndrome, the patient is circling the drain with septic shock and multiple organs failing

Therapy

- Regardless of "type," the treatment is the same: **Early Goal Directed Therapy**.
- This takes place in the ***first six hours of hospitalization*** (early) and is designed to ↑ **Tissue Perfusion**, ↓ **Tissue Hypoxia**, and **control the source.**
- Controlling the source begins by eliminating sources of infection (**IV sites, Abscess Drainage,** and **Wound Debridement**) and starting **empiric antibiotics** for the suspected agent.
- **Blood Cultures** should be drawn prior to antibiotics, but do NOT delay the treatment with broad-spectrum antibiotics.
- In order to meet tissue perfusion demands certain criteria should be monitored.
- To maintain **perfusion** (MAP > 65, CVP 8-16) a **30cc/kg bolus** is the first step.
- If responsive, nothing more needs be done.
- Failure of the fluid challenge will require the need for **pressors.**
- To maintain **oxygenation** (oxygen delive > oxygen consumption, or SvO2 > 70% both **oxygen** and **blood** (if Hgb < 7) should be given.

Early Goal Directed Therapy

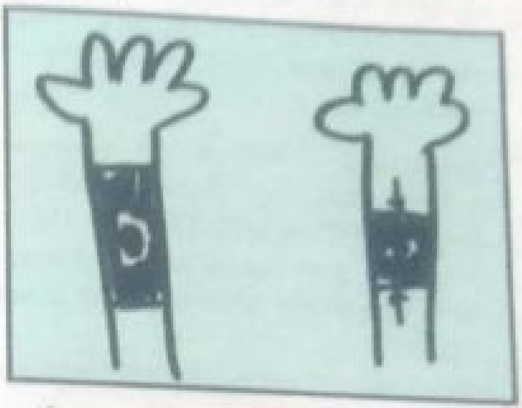
CVP	10-12mmHg
MAP	>65mmHg
Uoutput	>0.5/kg/hr
$SvcO_2$	>70%
1)	Give 300cc/kg IV Bolus
2)	Remove all source of infection
3)	O_2 as needed
4)	Pressors if fluid blous fails
5)	Empiric abx while waiting for culture



SKIN INFECTIONS

Cellulitis

- Cellulitis is an infection of the subcutaneous tissue of the skin.
- It's most often caused by infection by the skin flora: **Group A Strep** and **Staph aureus**.
- The presentation of a cellulitis is usually **red, hot, tender** skin that's often **well-demarcated** (i.e. you can draw a pen or marker on the edge and watch it grow or recede).
- It usually has a **portal of entry** (like a scratch, scrape, or puncture wound).
- The diagnosis is often clinical – it rarely requires culture or biopsy.
- If there's an **abscess** (likely to be **Staph**) it should be drained; culture the pus. But without purulent drainage there should **be no attempt to culture the cellulitis**, as what you'll likely receive is the polymicrobial sample of the skin.
- The treatment for cellulitis is affected by one of two scenarios. When the person **isn't toxic** and they walk into clinic without systemic signs of infection, a **1st generation cephalosporin** such as cephalexin, or antibiotics that'll cover community acquired MRSA such as **TMP-SMX** (Bactrim) or **Clindamycin** can be picked.



- If a person is toxic – there's **sepsis** - it's time to reach for the bigger guns such as **vancomycin** or **linezolid**.
- Daptomycin is an alternative.
- You know you're winning when the ring of cellulitis recedes towards the portal of entry. A failure to recede may indicate you have the wrong bug, the wrong drug, or that there's something under the skin that can't be seen.
- Routine imaging isn't required for cellulitis, but can be done when there's a failure to resolve.

Osteomyelitis

- Osteomyelitis is infection of the bone. This occurs via **hematogenous** seeding or by **direct inoculation** (trauma, fracture).
- If you can **probe to bone** through a wound, it's osteo. The other way to catch osteomyelitis is in a refractory or recurrent cellulitis.
- Diagnose with **X-ray**. If there's osteolytic changes, the diagnosis is made.
- It's often negative, because it takes two weeks to turn positive.
- If suspicion of osteo is high, but the X-ray is negative, the best radiographic test is **MRI**.

- Two tests that are usually the wrong thing to do are **Bone Scan** (useful only when there's no overlying inflammation) and **Tagged WBC scan,** which is always wrong. Once osteo is identified, take a **biopsy**. It's the best way to confirm osteo and is necessary to direct antibiotic therapy.
- **Treatment** is **4-6 weeks of antibiotics,** which is why the culture and sensitivity is wanted. Follow with **ESR** and **CRP** weekly to gauge the response to therapy. ***DO NOT repeat the MRI. DO NOT repeat the biopsy.***

Scenario	*Treatment*
Non-Toxic Outpatient	1st Gen Cephalosporin
Non-Toxic CA-MRSA	TMP-SMX, Clinda
Toxic (inpatient)	Vanc, Dapto, Linezolid

Osteomyelitis

Risk Factors	Bug
Most Common	S. aureus
Penetrating / Sneakers	Pseudomonas
Sickle Cell	Salmonella
Gardening	Sporothix
DM/PVD	Polymicrobial, cover for Pseudomonas
Oysters + Cirrhotic	V. vulnificus

Gas Gangrene

- Gas Gangrene is caused by **Clostridium perfringens.**
- The patient will present with some sort of wound, often a penetrating wound that gets **contaminated.**
- **Crepitus** will be able to be felt.
- The diagnosis begins with an **X-ray,** showing **gas** in the soft tissue.
- The treatment is **debridement** and **PCN + Clindamycin.**
- Gas gangrene is induced by a toxin, so clinda's ability to interrupt protein synthesis makes it ideal.

Necrotizing Fasciitis

- "Neck Fack" is a life threatening surgical emergency.
- It's caused by the same things that cause cellulitis: **Strep** and **Staph.** It presents as a really bad cellulitis.

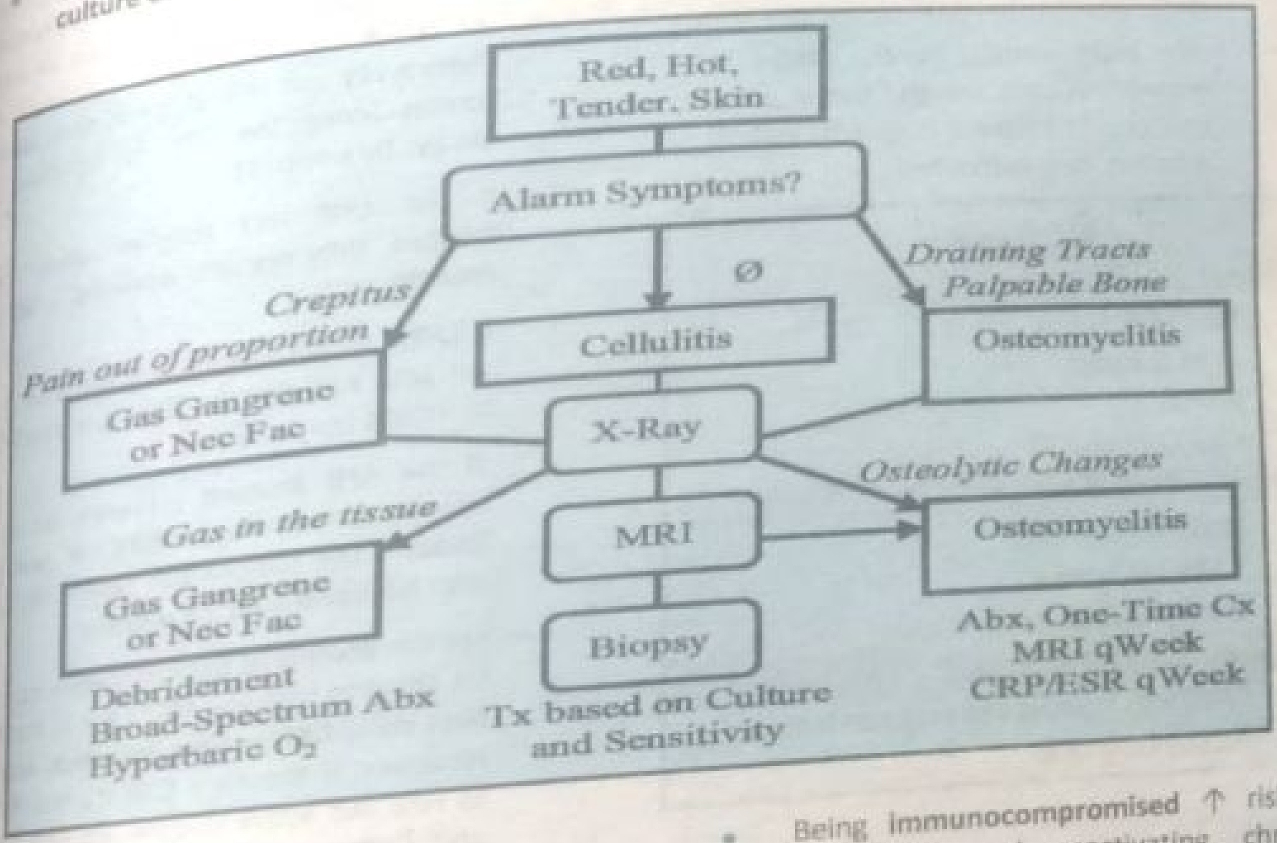
Look for a cellulitis that is:

1) **Rapidly progressive** with fast spread
2) **Crepitus**
3) **Pain out of proportion** with the physical exam
4) **Blue-Grey discoloration** of the skin
    - The diagnosis starts with **X-ray,** which will show gas in the tissues. We know from Gas Gangrene that we'll need to get **surgical debridement** right away.
    - If on a limb, often we simply amputate to prevent the spread of infection through fascial planes.
    - **Broad spectrum antibiotics** is required.
    - It's fatal if untreated.
    - If this process is occurring in the groin (male genitalia or female perineum) it's referred to as **Fournier's Gangrene.**

The Effective Workup

- When cellulitis is seen you want to think a little bit more about it. If they're non-toxic it's easy – treat empirically. But there are some things that should be on the radar, such as: **draining tracts** and **palpable bone** (osteo) or **crepitus** and **pain out of proportion** (gas gangrene or necrotizing fasciitis).
- The **x-ray** can reveal osteolytic changes of osteomyelitis, or the gas of the gas gangrene / nec fac. But, if nothing's found and there's still suspicion of Osteo, get an **MRI** of the bone plus a **biopsy if possible.**

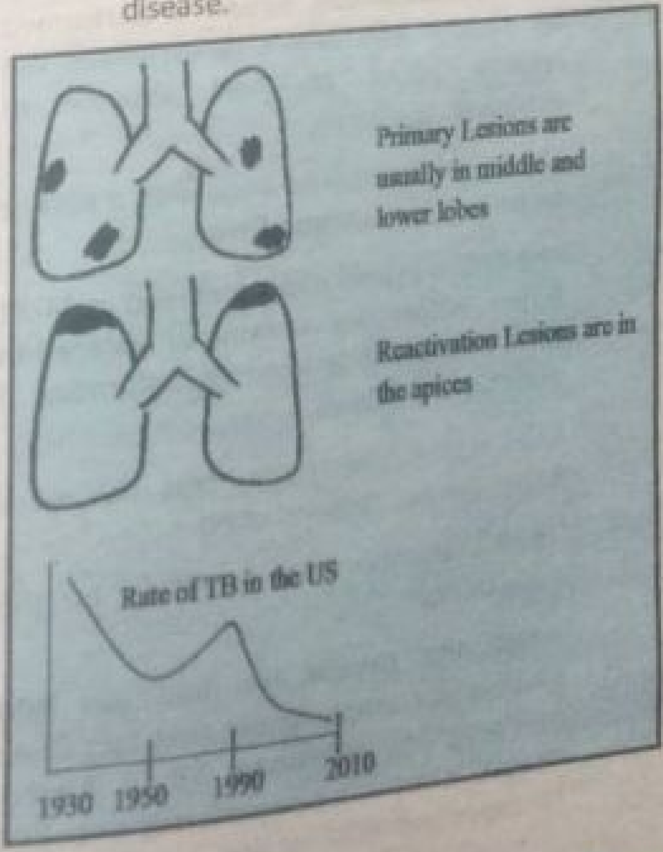
- Only give antibiotics to osteo **after the culture** or if the patient is **toxic**.
- Always give antibiotics to Gas Gangrene and Nec Fec.


Red, Hot, Tender, Skin
Alarm Symptoms?
Crepitus
Pain out of proportion
Ø
Draining Tracts
Palpable Bone
Gas Gangrene or Nec Fac
Cellulitis
Osteomyelitis
X-Ray
Osteolytic Changes
Gas in the tissue
MRI
Osteomyelitis
Gas Gangrene or Nec Fac
Biopsy
Debridement
Broad-Spectrum Abx
Hyperbaric O2
Tx based on Culture and Sensitivity
Abx, One-Time Cx
MRI qWeek
CRP/ESR qWeek

TUBERCULOSIS

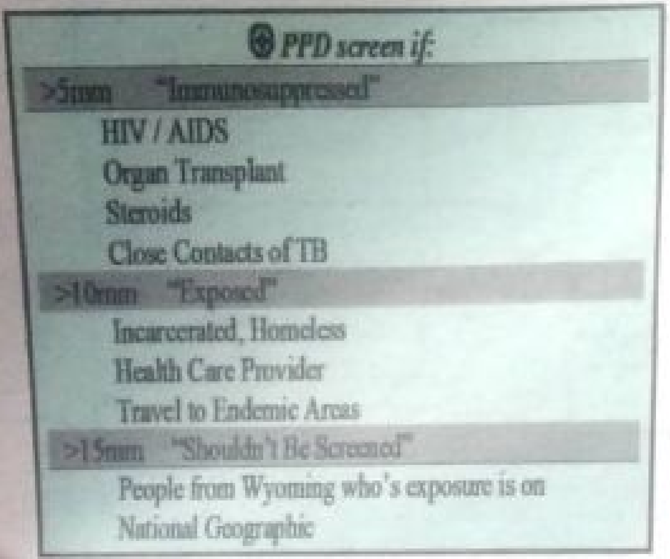
Microbiology and Epidemiology

- TB is an **acid-fast bacillus** that stains poorly on Gram stain.
- It's spread through the **aerosolized** respiratory droplets and infects the lungs.
- Primary TB presents like a pneumonia and localizes in the **middle or bottom** lobe.
- Unable to kill the bacteria, the body forms cavitary lesions (aka **caseating** granulomas) to wall off bacteria.
- **Reactivation** TB occurs in the ***apices*** – where *oxygen tension is highest.*
- Cavitation results in lung fragmentation and **hemoptysis.**
- Major risk for the spread of TB is a place where there are too many people in too small a space (**military barracks, prison,** and **homeless shelters**).
- Being **immunocompromised** ↑ risk of contracting and reactivating chronic disease.


Primary Lesions are usually in middle and lower lobes
Reactivation Lesions are in the apices
Rate of TB in the US
1930
1950
1990
2010

Patient Presentation

- There are **two types of patients**: those who are **asymptomatic** but exposed and those with cavitary pneumonia presenting with **night sweats, fever, weight loss, hemoptysis,** and cough. These patients are going to follow a diagnostic algorithm separate from each other.



⊕ *PPD screen if:*

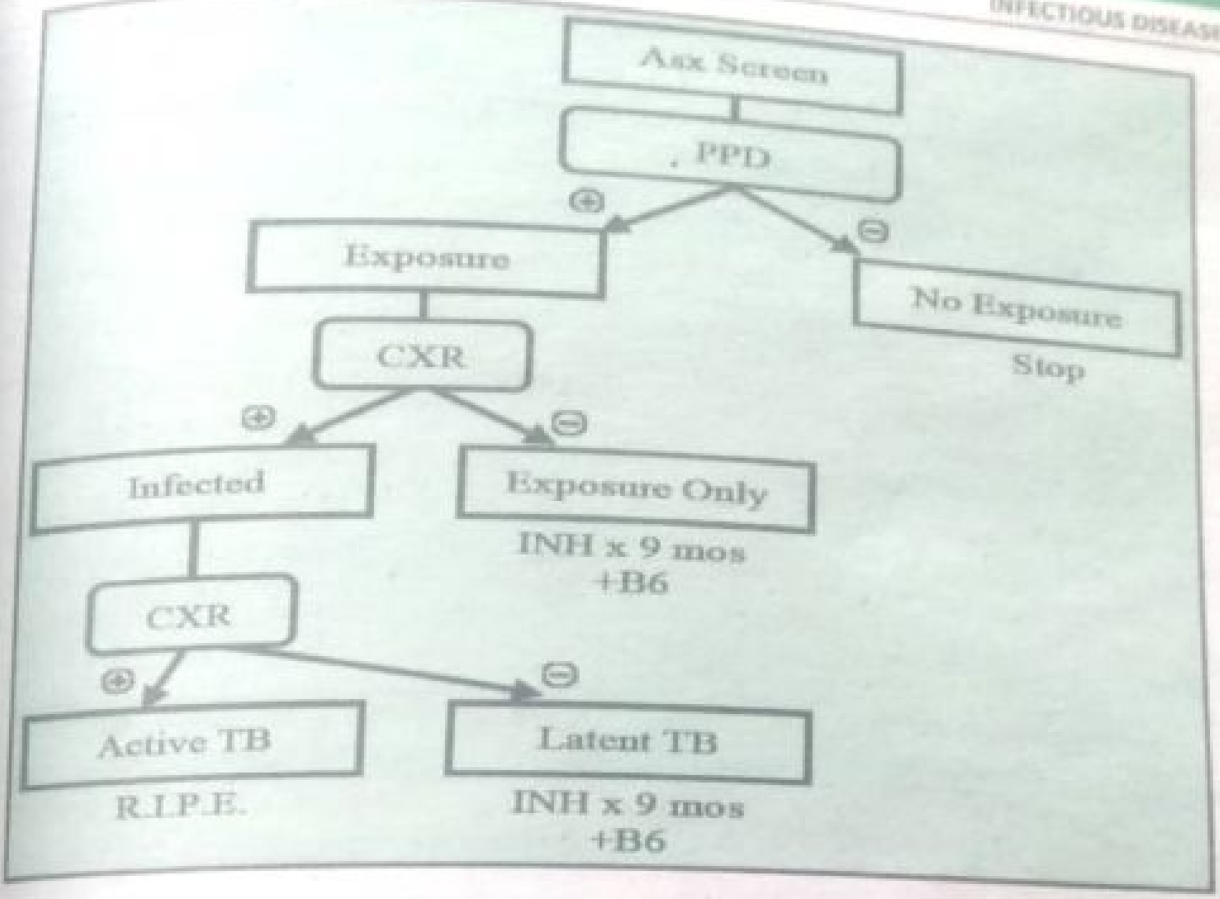
>5mm "Immunosuppressed"
HIV / AIDS
Organ Transplant
Steroids
Close Contacts of TB
>10mm "Exposed"
Incarcerated, Homeless
Health Care Provider
Travel to Endemic Areas
>15mm "Shouldn't Be Screened"
People from Wyoming who's exposure is on National Geographic

Diagnosis

- The **asymptomatic screen** is performed on people who aren't symptomatic but require proof of their absence of exposure.
- The initial test can be done with a **PPD** or an **Interferon-Gamma Assay**.
- The PPD is placed today and read in 48-72 hours, where the amount of **induration** (not erythema) is used to determine if positive or negative.
- The Gamma-interferon test is more expensive but tells yes or no.
- There's also no need to return for the assessment.
- When the patient has had the **BCG vaccine** you simply **ignore that fact** when assessing for pulmonary TB. If forced, choose interferon-gamma assay over PPD for those with BCG vaccine.
- If a patient is symptomatic, has a positive PPD, or a positive Gamma-Interferon Assay, a **chest x-ray** is required to assess for active disease. In these patients, the **chest x-ray** will also serve as their **annual screen** (once the PPD is positive, it'll always be positive).
- If the **CXR** and they've never been treated, they require **Isoniazid + B6** x 9 **months.**
- If **CXR⊕** an active infection must be ruled out with **AFB smears**. This is a good time to isolate the individual.
- If the **AFB Smear⊕** , there's an active infection; treat with **RIPE**. If the **AFB Smear** , the patient has latent TB; treat with **Isoniazid + B6 x 9 months.**
- For the **acutely ill patient** there's no need (or time) to wait the **48-72 hrs** of the PPD. **First** do a **CXR** looking for **apical lesions**. However, if there's a CXR it's insufficient to rule out active disease; an **AFB Smear** and **Culture** must also be done. If the ***disease is suspected*** a positive confirmation is desired.
- Send out **early morning** sputum and at least a **total of 3** cultures 8 hours apart. It's essential to ensure it's **negative** so also send out **3 early morning sputums 24 hrs apart**. For AFB smear culture **⊕(active disease)** treat with RIPE. ***If AFB smear look for another diagnosis such as malignancy***; it isn't TB that's causing the symptoms.
- The culture that's initially **negative**, but then comes back 6 weeks later **as positive** is non-tubercular mycobacterium. It's like **MAC– mycobacterium avian complex.**

Other Diagnostic Tests

- **Nucleic Amplification** can be used to ensure that the thing you thought was TB is really not TB. **Excellent sensitivity.**
- **Adenosine Deaminase** can be used in pleural effusions, and is **better** than an AFB smear and culture.


Asx Screen
PPD
⊕
⊖
Exposure
No Exposure
Stop
CXR
⊕
⊖
Infected
Exposure Only
INH x 9 mos +B6
CXR
⊕
⊖
Active TB
R.I.P.E.
Latent TB
INH x 9 mos +B6

reatment

- Anyone with a PPD⊕ or **CXR** is going to get at least 9 months **Isoniazid + B6**.
- For **active** disease we get a trial of **Rifampin**, Isoniazid, **Pyrazinamide**, **Ethambutol** (RIPE). It's a good idea to know the side effects of these drugs. **ALL 4 cause hepatotoxicity.**
- To treat non-tubercular mycobacterium (MAC) treat with Clarithromycin and Ethambutol.

IPE Side Effects(Note that hepatotoxicity is a side ffect for all)

ifampin	Red Urine
NH	Neuropathy (Give B6 Ppx)
yrazinamide	Hyperuricemia, Gout
thambutol	Eye Disturbance (optic neuritis)

URINARY TRACT INFECTIONS

Presentation and Background

- UTIs are infections involving anything from the kidneys to the urethra.
- It's most common in **women aged 18-24** because of their relatively **shorter urethra** (women) and **frequency of sex** (age group).
- **Sex**, **OCP**, and **Anal** intercourse all ↑ risk of infections.
- The UTI is most often caused by fecal flora coming into contact with the urethra. This means **E. coli** is likely to be the causative organism.

isease	*Symptoms*	*Test*	*Treatment*
[illegible]	Asx screen	U/A U_{Cx}	Pregnant: Amoxicillin

Bacteriuria	Procedure, Pregnant		Nitrofurantoin
Urethritis	pregnant U/A UCx Pregnant: Amoxicillin Nitrofurantoin Urethritis Frequency Urgency Dysuria + Discharge	U/A UCx + DNA	Ceftriaxone 125mg IM + Doxy 100 x 7 days or Azithro 250 x 1 po
Cystitis	Frequency Urgency Dysuria	Clinical	TMP-SMX or Nitrofurantoin or Fosfomycin
Pyelo	Frequency Urgency Dysuria + Fever + CVA Tender	U/A U_{Cx} B_{Cx}	IV Cephalosporin (inpt) or PO FQ (outpt)
Abscess	Pyelo that does not improve	CT or U/S	Drainage + Abx (same as Pyelo)

Urethritis

- Urethritis is Cystitis + **Urethral Discharge** - especially in a **sexually active** person. We no longer need the swab; simply just obtain **urinary Gc/Chla**.
- The urethral discharge is generally more disconcerting to the patient.
- The cause? Usually **STDs**.
- Treat **Gonorrhea** with **Ceftriaxone 125 IM x1** and treat **Chlamydia** with **Doxycycline 100 x 7days** or **Azithromycin 250 x 1**. *Treat both, even if you only find one.*

Asymptomatic Bacteriuria

- Bottom line, **don't treat asymptomatic bacteriuria**, defined as no symptoms but > 105 colonies.
- The exception to this are **pregnant females** and anyone with a **urologic procedure**.
- *If you screen AND there's a reason to treat (pregnancy or procedure) then yes, treat. But all other permutations are NOT treated.*
- On medicine, don't treat.

Pregnant Side Note
• Confirmation of eradication is required only in pregnancy. It's justified by being "another screen," > 2 infections means PPx Abx in pregnancies thereafter.

- On OB, do treat. In pregnancy, it's treated to prevent progression to pyelo and to clear GBS.
- Use **amoxicillin** as the front line agent and **nitrofurantoin** if penicillin allergic.

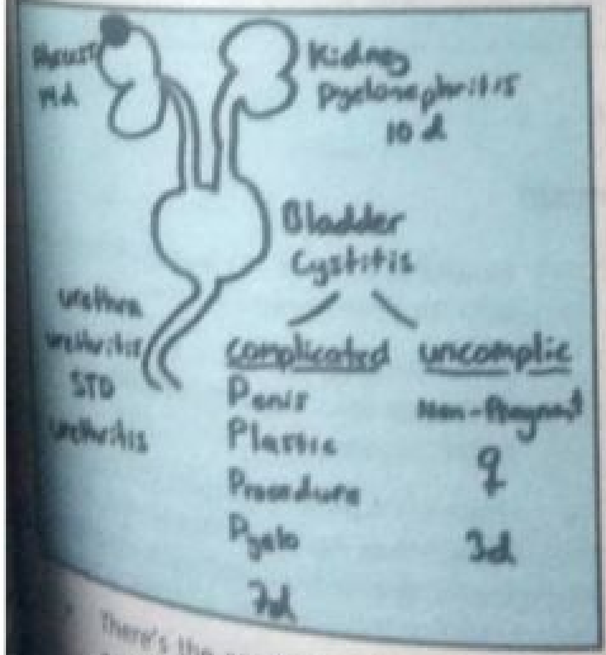
Cystitis

- Presenting with **frequency / urgency / dysuria**, cystitis ("bladder infection") is the most common of the UTIs.
- Systemic symptoms like N/V, Fever, and Chills are **absent**.
- The diagnosis is clinical.
- With a clear diagnosis it's fine to just treat.
- A urinalysis can be performed to confirm and cultures are almost always unnecessary.

- If it's an ***uncomplicated UTI***, treat for 3 days.
- If it's a **complicated UTI**, treat for 7 days.
- The antibiotics of choice are **TMP-SMX** (Bactrim), **Nitrofurantoin**, or **Fosfomycin**.
- Ciprofloxacin should NOT be used for cystitis.
- "Complicated" means the presence of any of the "Ps" listed to the right and below.

lonephritis

- Pyelonephritis should be considered a systemic disease, often presenting with florid infection.
- There will be **urgency, frequency,** and **dysuria** PLUS **CVA tenderness** and a **fever**. These patients are often **toxic**.
- The **U/A** will show **white blood cell casts** (pathognomonic for Pyelo).
- The **urine culture** will direct ongoing antibiotics.
- The learning pt is pyelo gets admitted and receives **IV Ceftriaxone** or **IV Amp + Sulbactam**. Bonus –


Abscess
I&D
Kidney
Pyelonephritis
10 d
Bladder
Cystitis
urethra
urethritis
STD
urethritis
complicated
Penis
Plastic
Procedure
Pyelo
7d
uncomplic
Non-Pregnant
♀
3d

- There's the condition called "ambulatory Pyelo" where a young healthy woman can tolerate po, so she gets **PO Cipro**.
- This is the only indication for PO Cipro on ***the board exams***.

Abscess

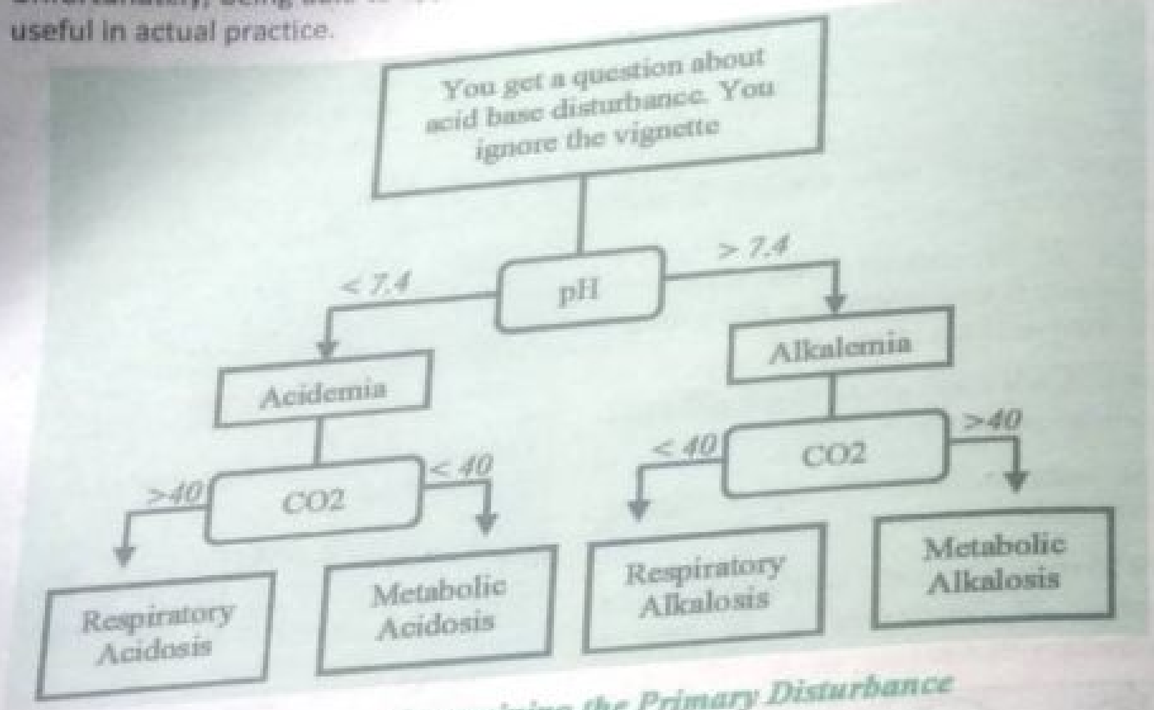
- The person who comes in with pyelonephritis who does **not improve** probably has an abscess.
- Either **CT scan** (preferred test) or an **Ultrasound** (if **pregnant**) will reveal it.
- **Drain it** and continue IV antibiotics.
- CT scan is best, but avoided in patients with **renal failure** or **pregnancy**.
- In those scenarios an ultrasound is an acceptable alternative.

Testing	*Notes*
U/A	Leukocyte Esterase Nitries
U Micro	+ WBC - Epithelial Cells
U Culture	Pregnant Procedure > 10^5 colonies = Treat Pyelo ?? Diagnosis, ?? Organism
CT	Screen for Abscess if non-pregnant
U/S	Screen for Abscess if non-pregnant

NEPHROLOGY

ACID BASE II – GAS INTERPRET

- Gas interpretation of acid-base disturbances is difficult.
- Unfortunately, being able to appropriately interpret a blood gas doesn't always prove incredibly useful in actual practice.


You get a question about acid base disturbance. You ignore the vignette
pH
< 7.4
> 7.4
Acidemia
Alkalemia
CO2
>40
< 40
CO2
< 40
>40
Respiratory Acidosis
Metabolic Acidosis
Respiratory Alkalosis
Metabolic Alkalosis

Determining the Primary Disturbance

Step 1: Acidemia or Alkalemia
Step 2: Respiratory or Metabolic
....
Step 3: is there something else wrong?

Follow the Steps

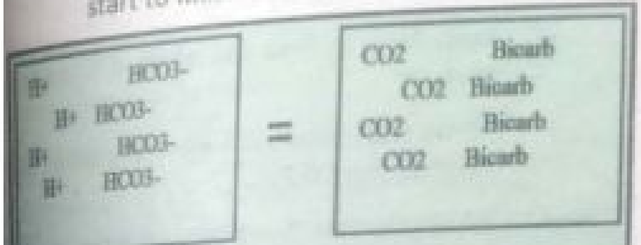
Step 1: Acidemia or Alkalemia. Use 7.4

- Is the pH < 7.4 **(acidemia)**
- Is the pH > 7.4 **(alkalemia)**

Step 2: Respiratory or Metabolic

- See CO_2 as respiratory and acid.
- CO_2 is the respiratory acid. If you get rid of CO_2 you get rid of respiratory acid; this should create an alkalotic environment. If you retain CO_2 you hold onto more respiratory acid; it should create an acidotic environment.
- After deciding if there's an Acidemia or Alkalemia ask, "What do I expect the CO_2 to be - high or low?"
- If there's a pH < 7.4, expect the CO_2 to be higher than normal - that is >40. If it is, the acidemia is caused by a respiratory acidosis. If it isn't, the acidemia is caused by a metabolic acidosis.

- If there's a pH >7.4, expect the CO_2 to be lower than normal (loss of respiratory acid).
- If it is, the alkalemia is caused by a respiratory alkalosis. If it isn't, the alkalemia is caused by a metabolic alkalosis.
- This step is SUPER important because it decides what Step 3 is going to be. Once the primary disturbance is determined you then go through that disturbance start to finish.



H+ = "Respiratory Acid" = pCO2

HCO3- = "Metabolic Base" = Bicarb

More H+ = More pCO2 = Low pH

Less H+ = Less pCO2 = High pH

More HCO3- = More Bicarb = High pH

Less HCO2- = Less Bicarb = Low pH

Step 3a: Check the anion gap.

- Always check the anion gap.
- It's normally 12.
- It's actually about 3* Albumin, normal albumin being 4, so this may change in real life.
- When handling acid-base problems, view them w/ the assumption of a normal anion gap = 12.
- The reason to always check the anion gap is because if present (regardless of other findings), there must also be an anion gap metabolic acidosis.
- That's true even if it isn't the primary disturbance.

Anion Gap = Na - Cl - Bicarb

Normal Anion Gap = 12... or Albumin x 3

If the calculated anion gap (Na-Cl-Bicarb) is greater than the normal anion gap there is an anion gap metabolic acidosis

REGARDLESS of whatever else is going

Respiratory Acidosis

Step 3b: Acute or Chronic

- If the respiratory acidosis is **acute** then for every dime change (every 10 points) of CO_2 the pH should change by 0.08.
- If the respiratory acidosis is **chronic**, then for every dime change of CO_2 the pH should change by 0.04. Step 3b is to find out which it is: **acute or chronic.**
- To do that, find out how many dimes from normal the CO_2 is.
- Multiply that by 0.08 and subtract from the normal pH of 7.4.
- Do it again multiplying by 0.04 and subtracting that from the normal pH of 7.4.
- Compare both scores to whatever the pH actually is. Whichever is closer determines the chronicity.

FOR EVERY "DIME" Change in CO_2

Δ pH	***Δ Bicarb***
If Acute 0.08	**If Acute 1**
If Chronic 0.04	**If Chronic 3**

Formula for memorizers:

7.4 - (Dimes * 0.08) = pH if acute

7.4 - (Dimes * 0.04) = pH if chronic

Pick the one closest to the actual pH

Step 3c: Is there a Metabolic Derangement

- For respiratory acidosis the bicarbonate should change as well.
- For every dime change in CO_2 the bicarb should change by 1 point if acute or 3

points if chronic. Bicarb should change to compensate for the CO_2; in a respiratory acidosis the bicarb should go up.

- Multiply the number of dime change of CO_2 by 1 (if acute) and by 3 (if chronic).
- Add that to a normal bicarb of 24.
- Compare to the bicarb you have.
- If there are more bicarbs than expected, there's also a metabolic alkalosis.
- If there are too few bicarbs, however, it's an additional metabolic acidosis.
- Note that in the example the CO_2 don't change. When exploring Step3c the only care is the bicarb number (too few, enough, too many).
- The CO_2 doesn't matter except to the extent that we use it to determine how much the bicarb should have changed.

Formula for memorizers:

24 + (dimes * 1) = Expected bicarb if acute

24 + (dimes * 3) = Expected bicarb if chronic

If actual bicarb > expected bicarb: too many bicarbs = Metabolic Alkalosis

CO2 Bicarb
CO2 Bicarb
CO2 Bicarb
CO2 Bicarb
Bicarb Bicarb

If actual bicarb < expected bicarb: not enough bicarbs = Metabolic Acidosis

CO2 Bicarb
CO2 Bicarb
CO2
CO2

Respiratory Alkalosis

- It's literally the same for respiratory acidosis, except that the bicarb changes by 2 (if acute) or 4 (if chronic) for every dime change.

Step 3b: Acute or Chronic

- If the respiratory alkalosis is **acute** then for every dime change (every 10 points) of CO_2 the pH should change by 0.08.
- If the respiratory acidosis is **chronic**, then for every dime change of CO_2 the pH should change by 0.04.
- Step 3b is to find out which it is: acute or chronic.
- To do that, find out how many dimes from normal the CO2 is.
- Multiply that by 0.08 and subtract from the normal pH of 7.4.
- Do it again multiplying by 0.04 and subtracting that from the normal pH of 7.4.
- Compare both scores to whatever the pH actually is. Whichever is closer determines the chronicity.

FOR EVERY "DIME" Change in CO_2

Δ pH	*Δ Bicarb*
If Acute 0.08	**If Acute 2**
If Chronic 0.04	**If Chronic 4**

Formula for memorizers:

7.4 + (Dimes * 0.08) = pH if acute

7.4 + (Dimes * 0.04) = pH if chronic

Pick the one closest to the actual pH

Step 3c: Is there a Metabolic Derangement

- For respiratory alkalosis the bicarbonate should change as well.
- For every dime change in CO_2 the bicarb should change by 2 point if acute or 4 points if chronic.

- Bicarb should change to compensate for the CO_2; in a respiratory acidosis the bicarb should go up.
- Multiply the number of dime change of CO2 by 2 (if acute) and by 4 (if chronic). Add that to a normal bicarb of 24. Compare to the bicarb you have.
- If there are more bicarbs than expected, there's also a metabolic alkalosis.
- If there are too few bicarbs, however, it's an additional metabolic acidosis.

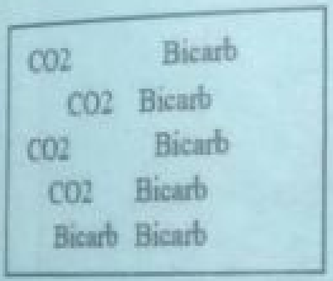
Formula for memorizers:

24 - (dimes * 2) = Expected bicarb if acute

24 - (dimes * 4) = Expected bicarb if chronic

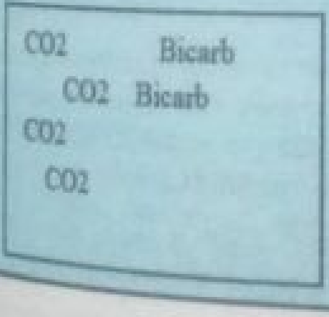
If actual bicarb > expected bicarb:

too many bicarbs = Metabolic Alkalosis



If actual bicarb < expected bicarb:

not enough bicarbs = Metabolic Acidosis



Metabolic Alkalosis

- The only way this will happen is if the aldosterone is up. Don't care about the gas interpretation, but instead whether it's "salt sensitive," which always means, "volume responsive," which also asks, "are they volume deplete?" To figure that out simply give the patient volume.

The way Metabolic Alkalosis will appear on an acid-base interpretation question is as a secondary disturbance to a respiratory problem or on its own. That's it.

Metabolic Acidosis

Step 3a: Check the anion gap. See above.

Step 3b: Is the CO2 appropriate for this bicarb?

- Assess if the pCO_2 on the ABG is appropriate for the bicarbonate. To do this, multiply the bicarb by 1.5 then add eight to that total. There is some fudge factor here. An cceptable range of pCO_2 is that number plus/minus 2.
- If the pCO_2 is in that range then there's no respiratory disturbance.
- If the pCO_2 is higher than that range, then there are too any respiratory acids, which means an additional respiratory acidosis.
- If the pCO_2 is lower than that range, there are too few respiratory acids, which means an additional respiratory alkalosis.

The Expected CO2 for Bicarb is Winter's Formula

$$\text{Expected CO2} = \textbf{Winters} = (\underset{\text{Bicarb you have}}{\text{Bicarb}} * 1.5) + \underset{\text{constant}}{8} \pm \underset{\text{fudge factor}}{2}$$

If actual CO2 > expected CO2:
too many CO2s = Respiratory Acidosis

CO2 Bicarb
CO2 CO2 Bicarb
CO2 CO2 Bicarb
CO2 Bicarb

If actual CO2 < expected CO2:
not enough CO2s = Respiratory Alkalosis

CO2 Bicarb
CO2 Bicarb
Bicarb
Bicarb

Add Back Method

$$\textbf{Actual } \underset{\text{Given to you}}{\textbf{Anion Gap}} - \textbf{Normal } \underset{12\ (\text{Alb} \times 3)}{\textbf{Anion Gap}} = \underset{= \text{Calculated}}{\textbf{Delta}}$$

Then...

Delta + given bicarb = expected bicarb

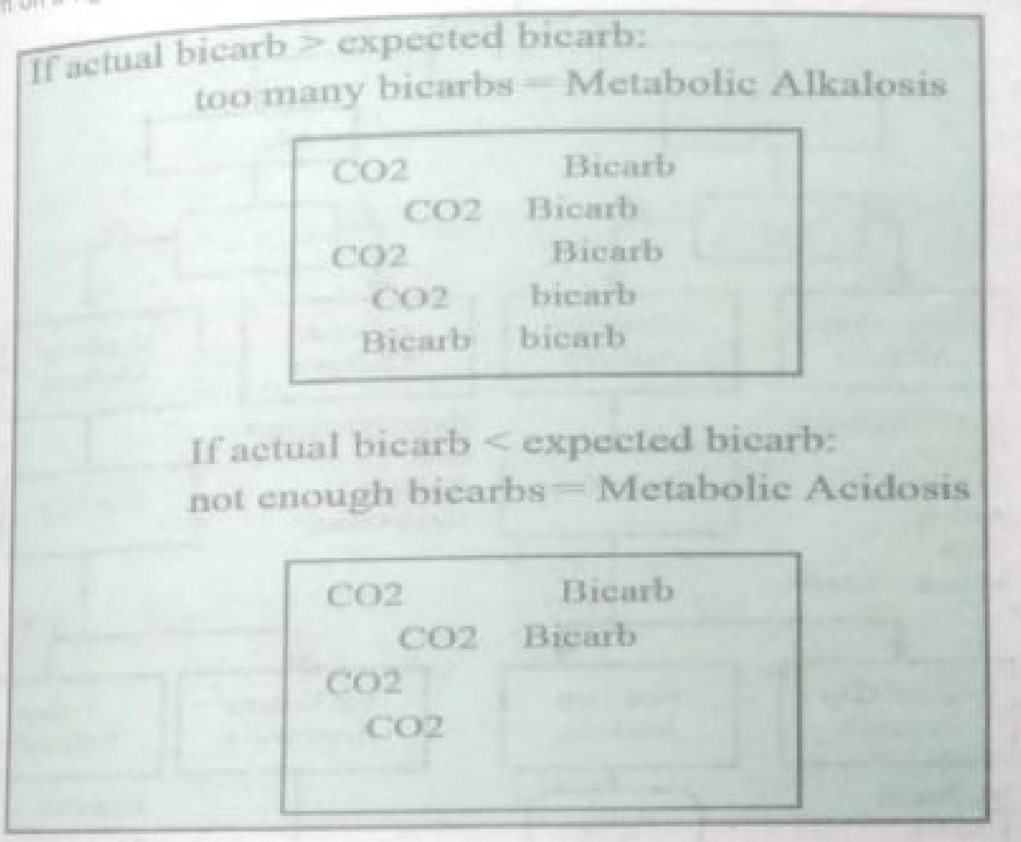
Step 3c: Is there another metabolic derangement?

- You'll read about the delta-delta. Stop reading about the delta-delta. It's simple to calculate but requires memorization to interpret. So we use the add-back method instead.
- A normal anion gap is 12. Take whatever the anion gap is right now and find out how many extra acids were needed to get there. Current Anion Gap - Normal Anion Gap. That number is the number of acids added to solution / the number of bicarbs that came out of solution. To find out how many bicarbs we started with before the anion gap business, add that number to the current bicarb.
- That value is how many bicarbs we started off with. normal is 24.
- If there are too many bicarbs (>24) there are too many metabolic bases – there's a additional metabolic alkalosis.
- If there are too few bicarbs (<24) ther are too few metabolic bases – there's

additional metabolic acidosis, because we started with an anion-gap acidosis, this must mean we have an additional non-gap metabolic acidosis.

- You'll be asked to do two things: interpret a blood gas which comes later and decide what to do next. We first handle "what to do next," the potential diagnoses that might be encountered and how to spot them on a vignette.

- The first step is to determine what the primary disturbance is. It's discussed in greater detail in gas interpretation, but basically <7.4 is acidic while >7.4 is basic. Then use the CO2 (with a cutoff of 40) to separate into respiratory or metabolic.



If actual bicarb > expected bicarb:
too many bicarbs = Metabolic Alkalosis

If actual bicarb < expected bicarb:
not enough bicarbs = Metabolic Acidosis

Respiratory Acidosis

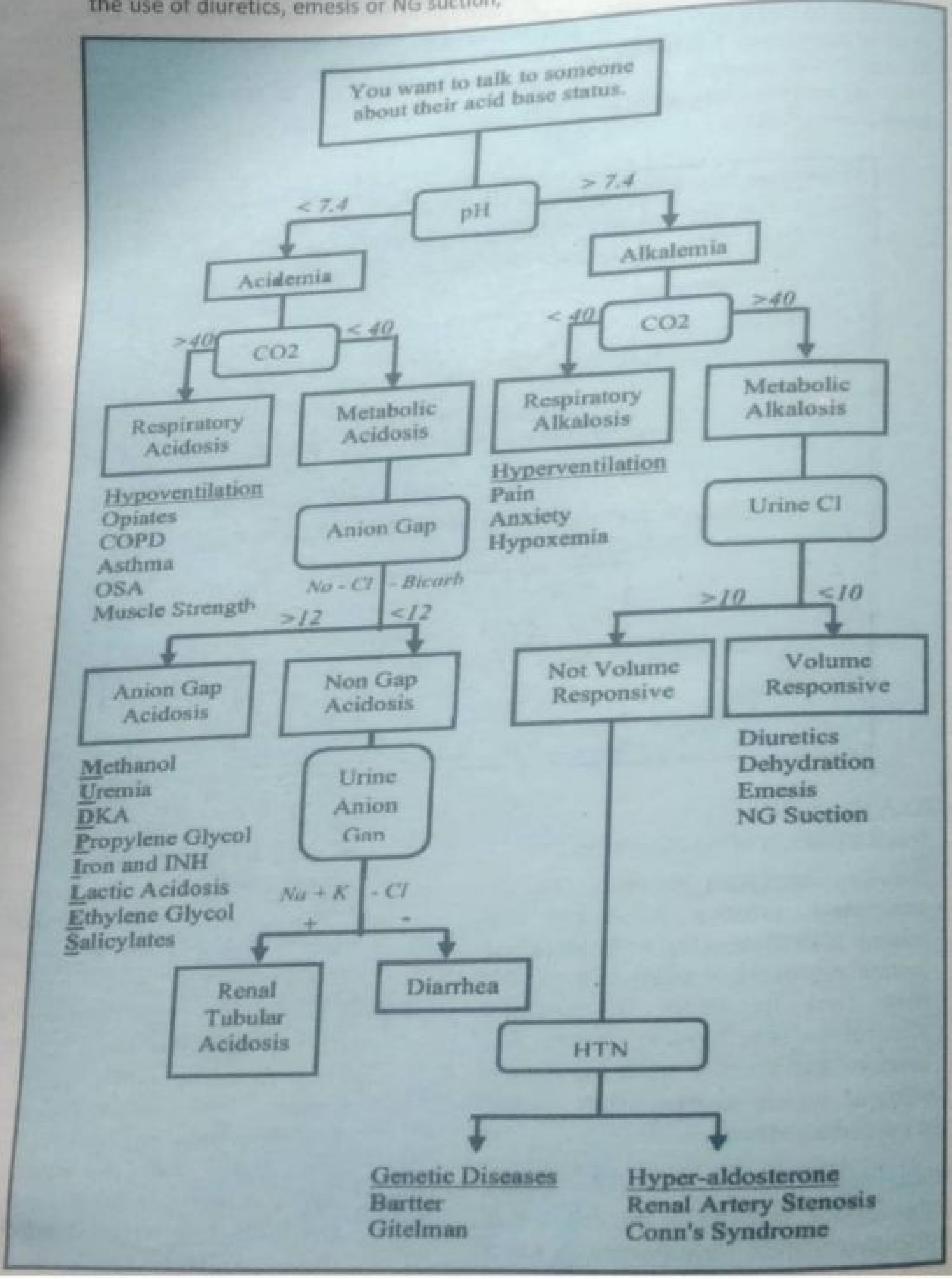
- This is a product of hypoventilation.
- The less ventilation he more CO_2 will accumulate. Whether it's a low tidal volume (COPD) or a low respiratory rate (opiate overdose), if either falls the CO_2 rises. Look for things like wheezing (Obstructive Lung Disease), obesity OSA), cyanosis and pinpoint pupils (opiates), or signs of muscle weakness (like paralysis from Guillain–Barré)

Respiratory Alkalosis

- Conversely, respiratory alkalosis is from hyperventilation. Very few things will do that as a primary disturbance. It'll either be pain, anxiety or hypoxemia. Lots of things cause hypoxemia (pneumonia, PE, ARDS) so the patient can get complex, but in terms of acid-base respiratory alkalosis means hyperventilation.

Metabolic Alkalosis

- The only thing that causes this is a high aldosterone. The decision is if the person is volume responsive - that is, will giving him/her volume improve their alkalosis? This is done in one of two ways: using the history to say he/she is volume down and give fluids, then recheck the bicarb R by checking the **urine chloride**. The test loves the urine chloride. If it's low (**<10**) the patient is salt sensitive, or volume responsive, and giving him/her volume will improve his/her condition. Look for the use of diuretics, emesis or NG suction, or another reason for them to be dehydrated (looking for insensible water losses like sepsis, fever, tachypnea, or tachycardia).


You want to talk to someone about their acid base status.
pH
< 7.4
> 7.4
Acidemia
Alkalemia
CO2
>40
< 40
Respiratory Acidosis
Metabolic Acidosis
Hypoventilation
Opiates
COPD
Asthma
OSA
Muscle Strength
Anion Gap
Na - Cl - Bicarb
>12
<12
Anion Gap Acidosis
Non Gap Acidosis
Methanol
Uremia
DKA
Propylene Glycol
Iron and INH
Lactic Acidosis
Ethylene Glycol
Salicylates
Urine Anion Gap
Na + K - Cl
+
-
Renal Tubular Acidosis
Diarrhea
CO2
< 40
>40
Respiratory Alkalosis
Metabolic Alkalosis
Hyperventilation
Pain
Anxiety
Hypoxemia
Urine Cl
>10
<10
Not Volume Responsive
Volume Responsive
Diuretics
Dehydration
Emesis
NG Suction
HTN
Genetic Diseases
Bartter
Gitelman
Hyper-aldosterone
Renal Artery Stenosis
Conn's Syndrome

Test	When To Use It
pH	Start here
pCO2	After pH to get primary disturbance
Anion Gap	Metabolic Acidosis
Urine Anion Gap	Non-Gap Acidosis
Urine Chloride	Metabolic Alkalosis

- If the Urine Chloride is high (**>10**) it's a condition that as nothing to do with volume. It's then time to assess for he presence of **hypertension**.
- If there is + **HTN**, consider diseases of too much aldosterone; inappropriate elevations in aldosterone levels. It's most likely to be renal artery stenosis or conn's syndrome (primary hyperaldosteronism). Keep in mind that the aldosterone was up in volume depletion to keep the pressure up. In this case it's up inappropriately, o it causes a rise in blood pressure.
- If the patient is - **HTN**, think of Bartter and Gitelman syndromes - genetic, always present forms of HCTZ and Furosemide, respectively.

- UCl < 10 = Volume Responsive
- UCl > 10 = Not Volume Responsive
- UCl > 10 and HTN = Inappropriate Aldosterone
- UCl > 10 and no HTN = genetic diseases

Metabolic Acidosis

- Metabolic Acidosis is the hardest to handle; it's the most complex by far in gas interpretation. But it's pretty easy to get the answer right when trying to make a diagnosis based on the clinical scenario.
- First, calculate the **anion gap** (Na - Cl - Bicarb). A normal gap is 12, or Albumin x 3. If greater, there's an anion gap acidosis, which can be reminded by a number of mnemonics. We've chosen MUDPILES in this section (just don't forget about Toluene). In an **anion gap metabolic acidosis** the diagnosis is made by the rest of clinical picture. Highlights of the ones you must know are to the right.
- For **non-gap acidosis** the next step is the **urine anion gap**. The urine anion gap is calculated from similar but not the same electrolytes as the regular anion gap (frustrating), so be careful. If **positive** the answer is renal tubular acidosis. If **negative** the answer is diarrhea.

URINE ANION GAP: Na + K – Cl (No Bicarb)

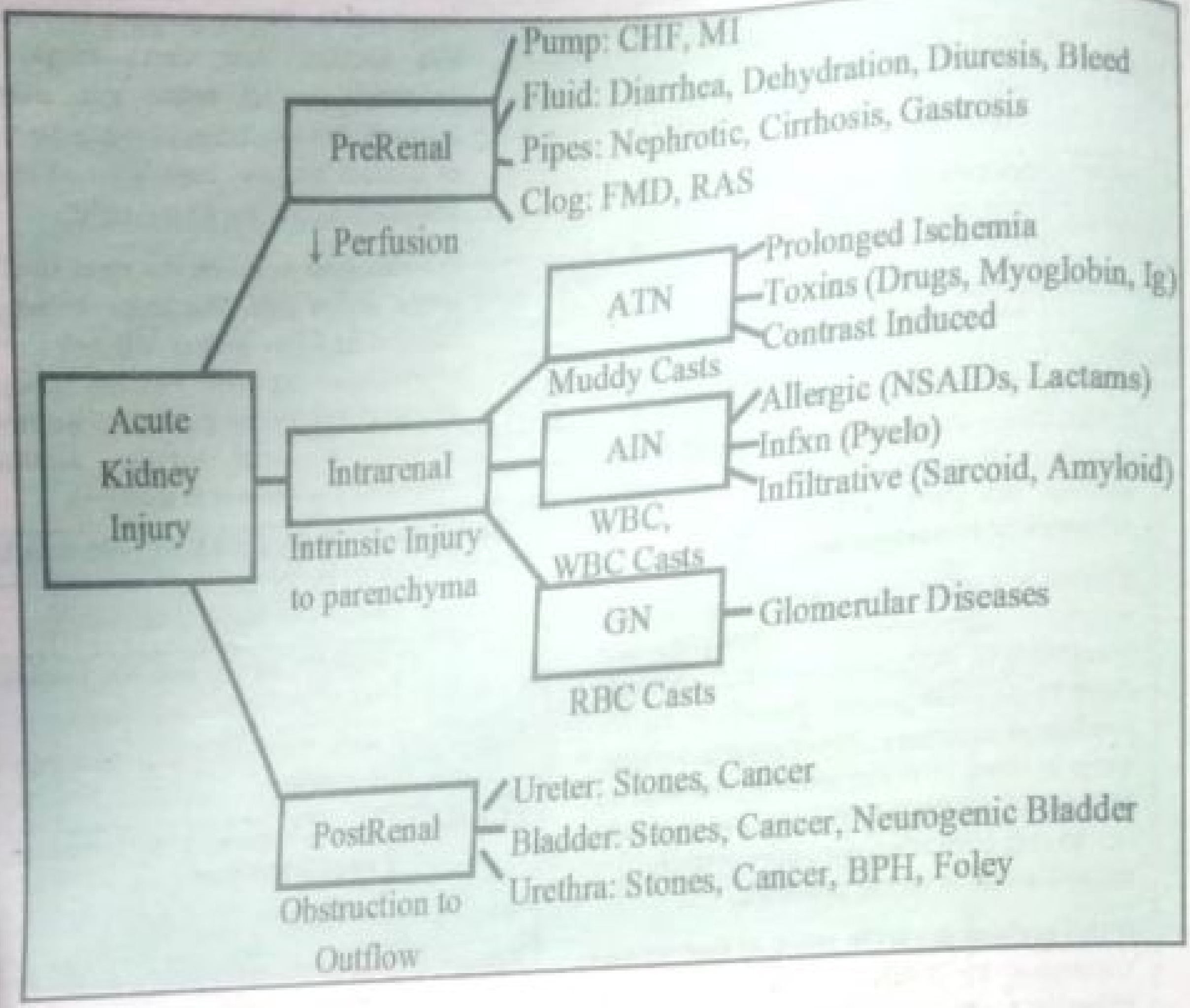
Highlights to MUDPILES Diagnoses

DKA	Diabetic who is acidotic. Look for ketones. Treat with insulin, fluids, and replete potassium
Methanol	Homemade liquor (moonshine), causes blindness, no cure
Ethylene	Crystals in the urine, urine turns color under Wood's Lamp. Give either ethanol or fomepizole
Lactic Acidosis	Either Metformin + Acute Kidney Injury or... Patient in shock (fix the shock)

ACUTE KIDNEY INJURY

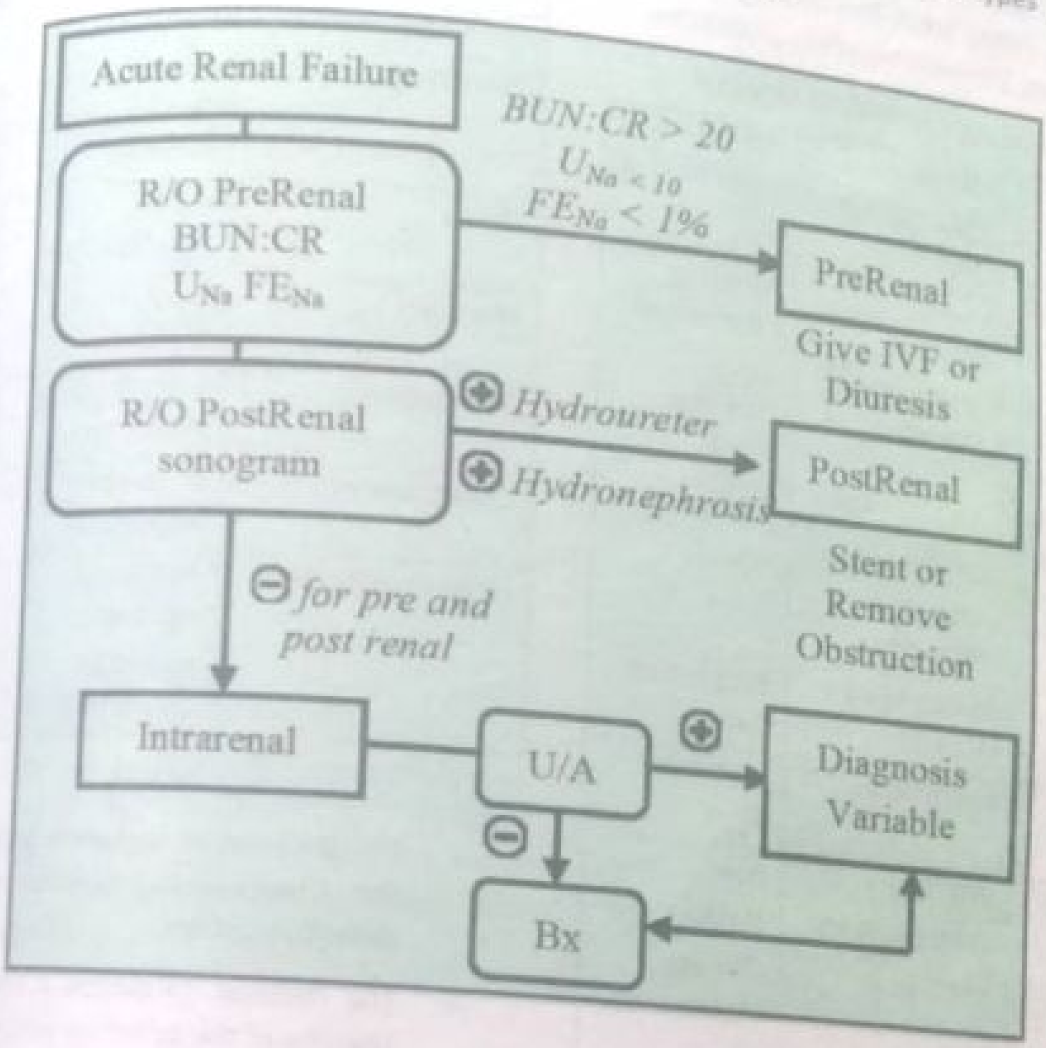
Approach to Renal Failure

- Renal failure, or **acute kidney injury**, often presents with only an **elevated creatinine** or **decreased urinary output**. Because the kidneys are redundant, unless the GFR gets very low the kidneys generally maintain near normal function. That is, until electrolytes get out of control the patient will be asymptomatic. It's usually on routine labs that it's encountered.


Acute Kidney Injury
PreRenal
↓ Perfusion
Pump: CHF, MI
Fluid: Diarrhea, Dehydration, Diuresis, Bleed
Pipes: Nephrotic, Cirrhosis, Gastrosis
Clog: FMD, RAS
Intrarenal
Intrinsic Injury to parenchyma
ATN
Muddy Casts
Prolonged Ischemia
Toxins (Drugs, Myoglobin, Ig)
Contrast Induced
AIN
WBC, WBC Casts
Allergic (NSAIDs, Lactams)
Infxn (Pyelo)
Infiltrative (Sarcoid, Amyloid)
GN
RBC Casts
Glomerular Diseases
PostRenal
Obstruction to Outflow
Ureter: Stones, Cancer
Bladder: Stones, Cancer, Neurogenic Bladder
Urethra: Stones, Cancer, BPH, Foley

- It's important to differentiate between **pre, post, and intra-renal failure**. The list of potential diagnoses is epic so it becomes prudent to develop a system.
- **Prerenal** is the result of **↓perfusion** - whether it be from ↓cardiac output, 3rd spacing of fluid, or ↓vessel diameter. In this case, the kidneys think they're dehydrated and **hold onto salt and urine**. Thus, the **urinalysis** will show a **low urine sodium** (**UNa<10**, **FENa<1%**) and a **BUN/Cr ratio > 20** (use **urea** instead of Na if a patient is on a diuretic). This should **also** always be the **first step** because it's very easy to fix (**IVF** if dry, **diuresis** if wet).
- **Prerenal Azotemia** (being a little dry) is the ***most common cause*** of acute kidney **injury** in the outpatient setting and should correct quickly with fluid.
- On the opposite side of the spectrum is **postrenal failure** from **obstruction to outflow**. Obstruction results in **hydroureter** or **hydronephrosis** and can be visualized by ultrasound. While CT can be used to diagnose obstruction, **ultrasound is the preferred test.** Obstruction can be at any level. **Stones and cancer** can cause obstruction throughout, but are most often in the ureters. **BPH, Neurogenic bladders,** and **kinked catheters** most often affect the distal GU system. The goal is to alleviate the obstruction, which can be done using various methods. Insertion of a **catheter** can relieve obstruction of the distal GU. **Stenting**, nephrostomy tubes, and rarely open surgery are used for the **proximal** GU system.

- **Intrarenal** disease is the last consideration. It can be quite difficult to diagnose. Definitive diagnosis can be made with a **biopsy,** but biopsy is rarely (if ever) the right answer. Instead, use of the **clinical history** and the **urinalysis** often provide the diagnosis. **Casts** are particularly helpful in differentiating between the three types of intrarenal disease.


Acute Renal Failure
BUN:CR > 20
U_Na < 10
FE_Na < 1%
R/O PreRenal
BUN:CR
U_Na FE_Na
PreRenal
Give IVF or Diuresis
R/O PostRenal
sonogram
⊕ Hydroureter
⊕ Hydronephrosis
PostRenal
Stent or Remove Obstruction
⊖ for pre and post renal
Intrarenal
U/A
⊕
⊖
Diagnosis Variable
Bx

[illegible]

Once honed to Intrarenal, the damage can be thought of in 3 distinct regions:

1) Tubules (Acute Tubular Necrosis)

- **Acute Tubular Necrosis** is caused by either **ischemic damage** or **toxin exposure**. The tubules necrose, die, and slough off. They form the shape of the tubules and present as **muddy brown casts**. They'll go through three phases: the **prodrome** where creatinine rises but urine output remains the same, an **oliguric phase** where creatinine rises and urine output plummets (caution fluid overload), and a **Polyuric phase** where the patient pees a lot. Through this time they need supportive care.

a. Contrast Induced ATN

- If a patient has **pre-existing renal damage** or is at increased risk, and they NEED contrast, give **vigorous hydration**, prophylactic **N-Acetyl-Cysteine**, and **Stop ACE/ARBs** and **Diuretics** prior to contrast. Dialysis is ineffective at preventing contrast induced nephropathy.

2). Interstitium (Acute Interstitial Nephritis)

- AIN is essentially an allergic reaction with invasion of white cells. **Drugs**, **Infections**, and **Deposition Disease** can cause it. The urine will present with immune cells: **white blood cells, white cell casts** (pyelonephritis), or **eosinophils**. Removal of the offending agent is crucial. That means either **treat the infection** or stop **the drug**. Steroids are often ineffective.

Urinalysis Findings

Pre-Renal	BUN/CR > 20, UNa < 10; FENa < 1%	IVF if dry Diuresis if wet
Post-Renal	Urinary Retention Hydronephrosis / ureter	Alleviate Obstruction: Catheter, Stent, Surgery
Intra-Renal	BUN/CR <10, UNa > 20; FENa> 1%!	
ATN	Muddy Brown Casts	Supportive Care
Allergic Nephritis	Eosinophilia	Remove Drug
Pyelonephritis Myoglobin Nephritis Glomerulo-nephritis	WBC Casts ⊕ Blood, Ø RBC RBC Casts	Abx $NaHCO_3$, IVF Disease Dependent
Gout	Uric Acid Crystals	Treat the Gout!

3) Glomerulus (Glomerulonephritis)

- A patient with **RBC casts** on urinalysis is indicative of glomerulonephritis. There are a crap-ton of diseases that can cause it. The way to tell them apart is with a **biopsy** – something not often done. Learning the typical histories should be enough. What becomes important is to ***rule out* Nephrotic Syndrome** (>3.5g/24hr urine, Edema, and Hyperlipidemia) with a **U/A Spot Test** or **24-hr urine**. This isn't step 1 stuff so don't worry about spending time memorizing biopsies, stains, or complement levels.

Glomerulonephritis	***History***	***Blood Test***
IgA Nephropathy	Post-Viral	
Post-Streptococcal	Post Pharyngitis / Impetigo	ASO titer
Lupus	⊕ANA, ⊕dsDNA, Sxs	⊕ ds DNA
Wegener's	Sinus, Lung, Kidney	⊕ ANCA
Goodpasture	Hemoptysis + Hematuria	⊕ Anti-GM
Churg-Strauss	Asthma + Hematuria	
Henoch-Schonlein	Post-Viral (IgA) and systemic vasculitis	

Acute Indications for Dialysis

- The decision to dialyze is NOT based on the Creatinine! **Transplant** is another definitive option.
- The decision to dialyze is based on the severity of the condition and the presence of one of the AEIOU mnemonic.

AEIOU mnemonic.
Indications for Dialysis:

- **A** Acidosis
- **E** Electrolytes (Na/K)
- **I** Ingestion (Toxins)
- **O** Overload (CHF, Edema)
- **U** Uremia (Pericarditis)

DISORDERS OF CALCIUM

Introduction and Physiology

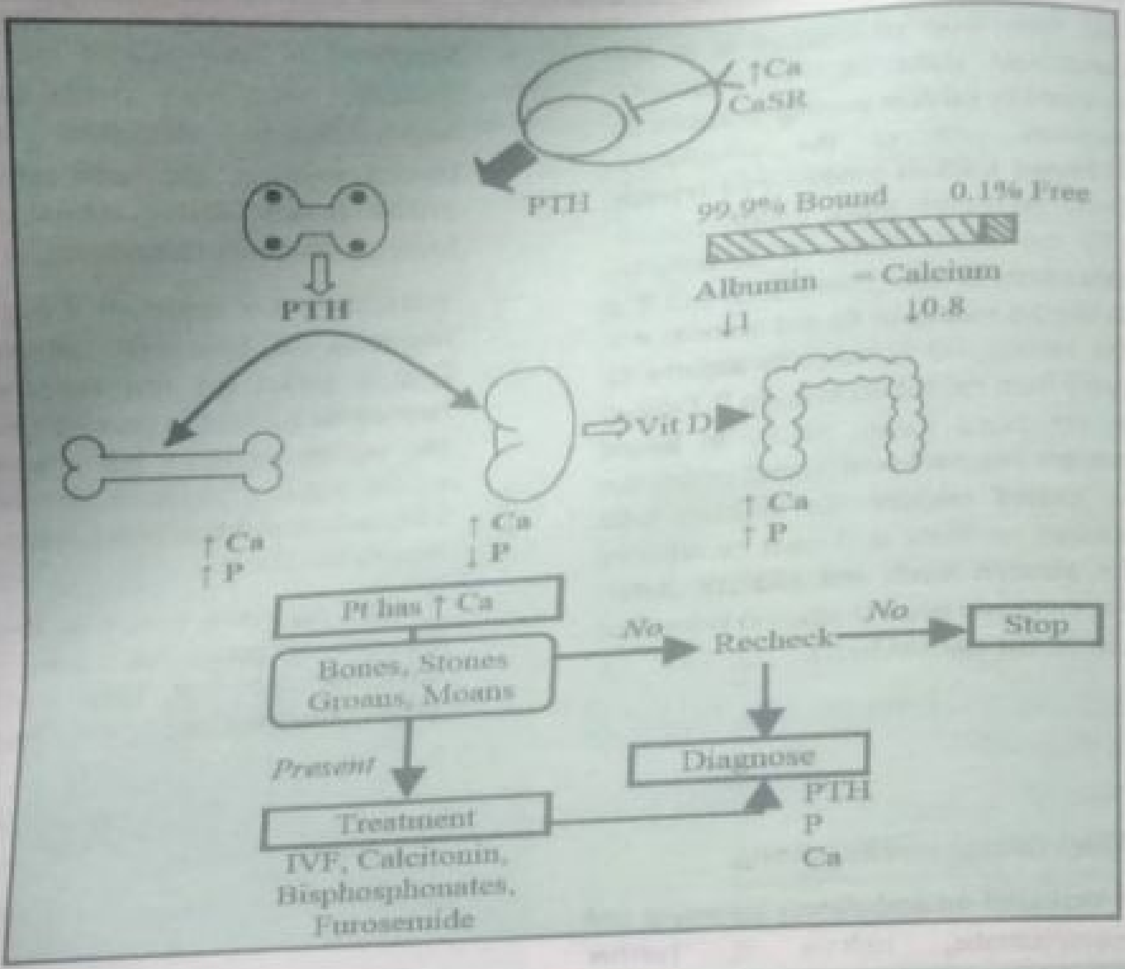
- Calcium is regulated by **Calcitonin** ("calci-tone-down") and by **parathyroid hormone**.

- The main level of function is at the parathyroid gland via PTH. Calcium's detected by **calcium sensing receptors** on secretory cells of the parathyroid. **Increased Calcium inhibits PTH release.** Thus, decreased levels permit release. PTH has three effects: it 1) activates **osteoclasts** to clear bone, **↑ Ca** and **↑ P** 2) directly **reabsorbs Ca** and **excretes P** in the kidney, and 3) indirectly **absorbs Ca** and P from the gut via **Vitamin D**. Calcium in the blood travels mostly as **bound calcium** (inactive) with a small proportion as **ionized calcium**. We measure **total calcium** routinely so it must be adjusted for **albumin levels** and **alkalotic states.** For every one point of albumin below four correct the calcium by 0.8.

every disease you'll use the PTH, Ca, and P
vel to make a diagnosis.

Hypercalcemia

- A high calcium may be nothing.
- If increased on ambulatory screening and asymptomatic, redraw it. Further investigation's required if it's still increased on the redraw or there are symptoms.
- **Symptoms** of hypercalcemia are: **bones** (fracture, osteopenia), **stones** (calcium Nephrolithiasis), **abdominal groans** (nausea vomiting, abdominal pain), and **psychic moans** (altered mental, severe hypercalcemia only, Calcium of 13-15).
- Diagnosis is less important if there are symptoms, so treat first. **Intravenous Fluid** is always the first line therapy. **Furosemide** is added to increase naturesis and calcium excretion, but only **AFTER** volume status is corrected (dehydration from early administration of furosemide is actually HARMFUL).
- If more aggressive therapy is required (because symptoms are severe), start **Calcitonin** (acts fast, fades fast) and **Bisphosphonates** (long term therapy).


↑Ca
CaSR
PTH
99.9% Bound
0.1% Free
Albumin
= Calcium
↓1
↓0.8
PTH
Vit D
↑Ca
↑P
↑Ca
↓P
↑Ca
↑P
Pt has ↑Ca
Bones, Stones
Groans, Moans
No
Recheck
No
Stop
Present
Diagnose
PTH
P
Ca
Treatment
IVF, Calcitonin,
Bisphosphonates,
Furosemide

Treatment	*Onset*	*Effect*
IVF	Rapid	Dilutes Calcium, ↑Prerenal Excretion via diuresis
Furosamide	Rapid	↑Diuresis = ↑Ca excretion. Use only after IVF
Calcitonin	Immediate	Effect fades quickly, gets you through a crisis
Bipshos-phonates	Chronic	Puts the calcium back on bone, risk of jaw osteonecrosis, good for fractures only

I. 1° Hyperparathyroidism

- **A single autonomous gland** secretes PTH without effective feedback. Calcium is absorbed (↑ **Ca**) while Phos is lost (↓P). An additional bone finding is found here - **fibrosa cystica** (aka "**brown tumor**") - from overstimulated osteoclasts creating large bone lesions.
- The treatment is **resection.**
- Use a **radionucleotide scan** to identify which gland is autonomous / hypertrophied.
- Monitor for signs of **hypocalcemia** after surgery (**hungry bone syndrome**).

II. 2° Hyperparathyroid

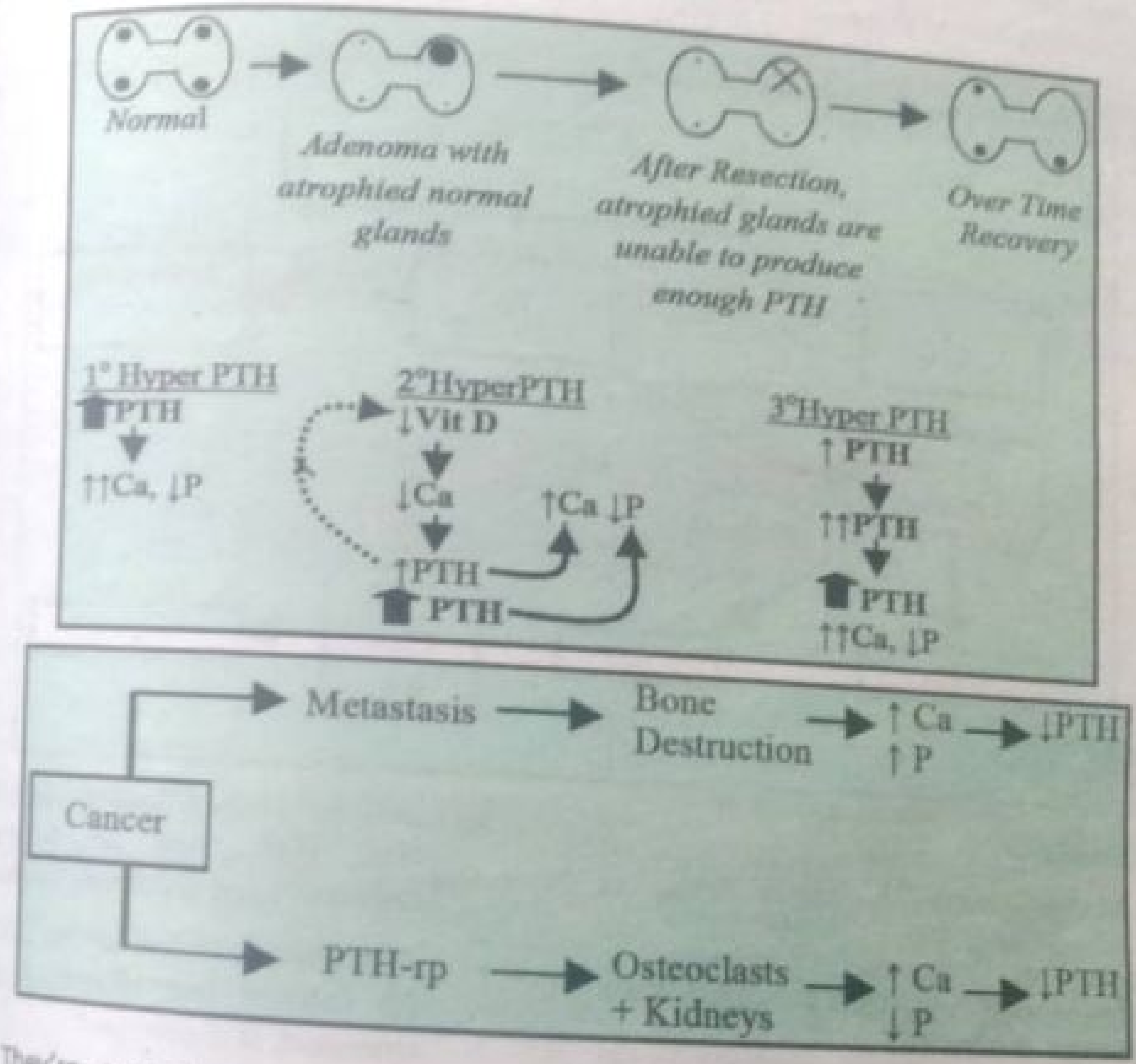
- In **early renal failure** Vit D isn't made.
- This produces a **hypocalcemia** that then causes **↑PTH** and **parathyroid gland hypertrophy**.
- PTH increases in order to maintain a normal calcium.

III. 3° Hyperparathyroid

- If renal failure continues, eventually **parathyroid glands** become **autonomous** - just like in primary hyperparathyroidism.
- This is an autonomous gland in the **presence of existing renal disease.** Although **resection** is required, there's no risk of cancer.

iv. Familial Hypocalciuric Hypercalcemia

- Caused by an **abnormal calcium sensing receptor,** there's a new "set point."
- There's an ↑**Ca** and ↑**PTH,** but the body is just maintaining its "normal."


Normal
Adenoma with atrophied normal glands
After Resection, atrophied glands are unable to produce enough PTH
Over Time Recovery
1° Hyper PTH
⬆PTH
↑↑Ca, ↓P
2°HyperPTH
↓Vit D
↓Ca
↑PTH
⬆PTH
↑Ca ↓P
3°Hyper PTH
↑ PTH
↑↑PTH
⬆PTH
↑↑Ca, ↓P
Cancer
Metastasis
Bone Destruction
↑ Ca
↑ P
↓PTH
PTH-rp
Osteoclasts + Kidneys
↑ Ca
↓ P
↓PTH

- They're **asymptomatic** and require **no treatment.**
- There's caution with stenotic aortic disease as they age.

Malignancy

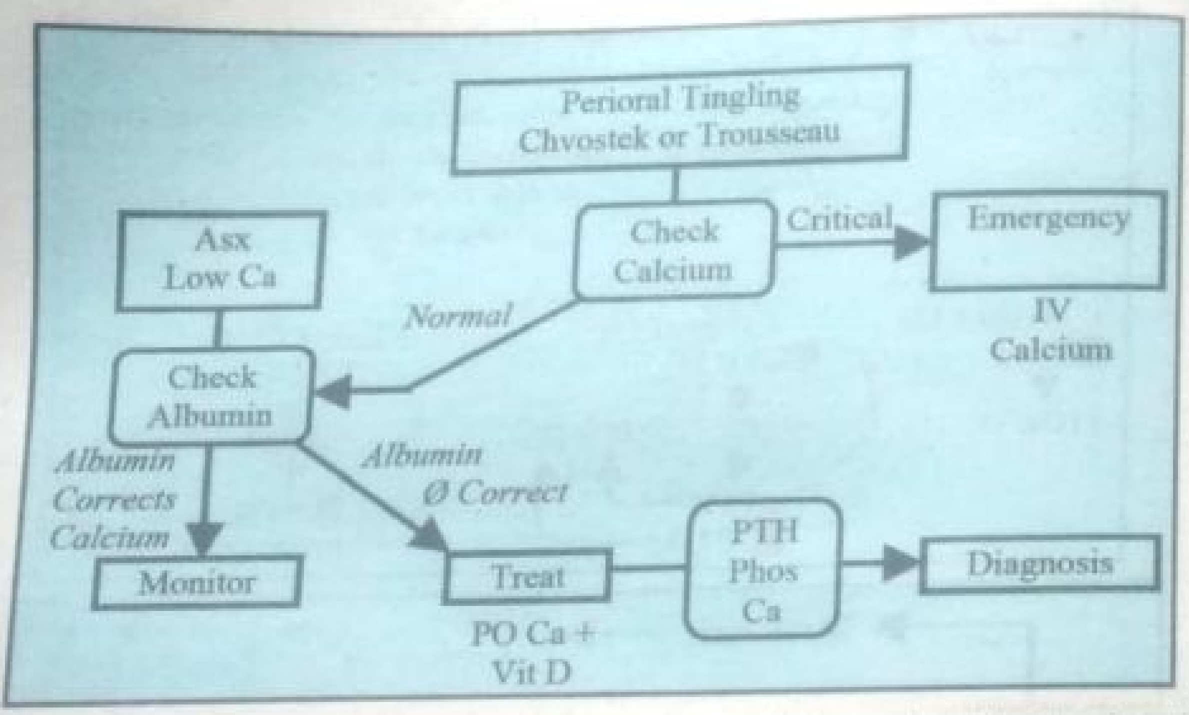
- Cancer can cause hypercalcemia. It can do it in two ways. Either **metastasis** goes to the bone and actively destroys it (releasing Ca and P) or a cancer can produce **PTH-rp** (parathyroid like hormone), turning the cancer into a 10 hyperparathyroidism but with a "low" blood PTH (our tests only captures the real PTH; special tests are required to measure levels of PTH-rp).
- Treat the cancer and the condition goes away.

vi. Immobilization

- For some reason (we think it's ↓ **impact stress**) patients who are **bed-ridden** have an **asymptomatic increase** in **calcium** secondary to bone turn over.
- Get them out of bed and walking - the condition will improve.

vii. Vitamin D excess

- **Granulomatous** disease (Sarcoid, TB) can turn on **Vitamin D independently** of kidneys, which increases calcium, turning off PTH, resulting in P being unable to be renally excreted. Use **steroids** to treat the underlying disease.


Perioral Tingling
Chvostek or Trousseau
Check Calcium
Critical
Emergency
IV Calcium
Asx Low Ca
Normal
Check Albumin
Albumin Corrects Calcium
Monitor
Albumin Ø Correct
Treat
PO Ca + Vit D
PTH Phos Ca
Diagnosis

2) Hypocalcemia

- **Albumin** plays a bigger role in Hypocalcemia.
- Poor nutrition, cirrhosis, or nephrosis will cause a ↓ **Albumin**.
- Adjustment for albumin usually reveals a **normal calcium**.
- Potentially, checking for **signs and symptoms** is important as it could lead to catching a life-threatening emergency before it gets there.
- Look for perioral tingling (usually comes first) then signs of **tetany** (both **Chvostek's** and **Trousseau's sign**).
- Treatment is to replace the calcium. Use **PO Calcium** and **Vitamin D** for **non-emergent, IV** if **emergent**.

i. Hypoparathyroidism

- Typically **iatrogenic**, either from an "oops" Thyroidectomy or from a parathyroidectomy of an adenoma (**hungry bone syndrome**) secondary to decreased PTH production of atrophied glands.

Ca	PTH	Disease	PO_4	Path
↑	↑↑	Hyperparathyroidism	↓	↑PTH = ↑Ca
	↑	FHH	↓	↑PTH = ↑Ca
	↓	Malignancy Mets	↑	↑Ca = ↓PTH
		Malignancy PTH-rp	↓	↑Ca = ↓PTH
		Immobilization	↑	↑Ca = ↓PTH
		Vit D Excess	↑	↑Ca = ↓PTH
↓	↑↑	Pseudohypoparathyroidism	↑	"Ø PTH"
	↑	Vit D Deficiency	↓	↓Ca = ↑PTH
		Chronic Renal Failure	↑	↓Ca = ↑PTH
		Pancreatitis	↓	↓Ca = ↑PTH
	↓	Hypoparathyroidism	↓	↓PTH = ↓Ca

Vitamin D Deficiency

- Whether it's from **renal failure** or **sunlight / diet deprivation,** having too little Vitamin D leads to secondary hyperparathyroidism. Initially, there's decreased calcium.

Calcium Sequestration

- An acute condition that's often in the setting of **pancreatitis.**

Pseudohypoparathyroidism

- An awfully named disease that means **PTH-end organ resistance**. There's a high PTH but everything works normally.
- Ignore it.

HRONIC KIDNEY DISEASE

onic Kidney Disease (CKD)

- When the creatinine remains elevated and won't come back down, it's a case of CKD.
- It's usually **>3 months of reduced GFR** (<60mL/hr, or a Creatinine ~2).
- The stage of renal disease is based on the GFR. We use the **creatinine as a surrogate** for GFR.
- There are a number of equations that can be used to estimate the GFR by the creatinine, but to use any of them the creatinine must be stable.
- That is, only in chronic kidney disease can you use the Creatinine to estimate the GFR.
- The overall management of chronic kidney disease is to **prevent progression** and **manage complications**.

Prevent progression

- **Hypertension** and **Proteinuria** are managed with **Ace inhibitors** and **Angiotensin Receptor Blockers.**
- Use either an ACE-I or an ARB – don't combine them. The blood pressure goal in CKD remains more aggressive than traditional hypertension management; it's **<130 / <80**.
- **Diabetes** is managed similarly.
- **All diabetics require annual urinalysis to assess for microalbuminuria. The A1c goal remains < 7.0. Caution must be used in CKD as insulin is renally excreted.**

Manage Complications

- **Anemia** results from decreased **erythropoietin.**

- The goal hemoglobin is 11-12.
- Anemia in CKD is usually normocytic and seen in late stage disease.
- Use **Erythropoietin** and **Iron supplementation** to sustain blood counts. Transfusions with dialysis can also be done.
- **Secondary hyperparathyroidism** is a **product of phosphate retention** (elevated phosphorous stimulates PTH) and **Vitamin- D Deficiency** that leads to low calcium (low calcium stimulates PTH). Thus, **phosphate binders** such as sevelamer and **calcimimetics** such as cinacalcet are used to decrease this risk.
- Chronic Kidney Disease Mineral Bone Disorders from secondary hyperparathyroidism can be protected against by giving **Calcium** and **1,25-Vitamin D** supplementation.
- **Volume Overload** is caused by the loss of urinary output. Initially, stimulation of the nephron can be sustained using **loop diuretics** such as furosemide. Combination therapy with metolazone and furosemide is a last ditch effort to maintain adequate urinary output. Ultimately, dialysis manages volume overload.
- Acidosis results in a bicarb between 12-20. **Bicarbonate** supplementation is used to reverse this.

Stage	*Description*	*GFR*	*Tx Goals*
I	Ø GFR effect	>90	Comorbidities
II	Mild	60-89	Comorbidities
III	Moderate	30-59	Comorbidities / Complications
IV	Severe	15-29	Prepare Dialysis / Transplant
V	Kidney Failure	<15	Dialysis required for survival

Intervention	*Goal*	*Progression*
ACE-inhibitor	BP <130/ < 80	HTN
Insulin	bG 80-110	DM

Complication	*Goal*	*Example*
Anemia	Hgb> 10	EPO, Iron
Secondary Hyperparathyroidism	PTH	Calcimimetics Phos Binders
Osteoporosis	Dexa >-2.5	Ca, 1.25VitD
Volume Overload	None	Loops Hemodialysis
Metabolic Acidosis	Bicarb > 20	NaBicarb

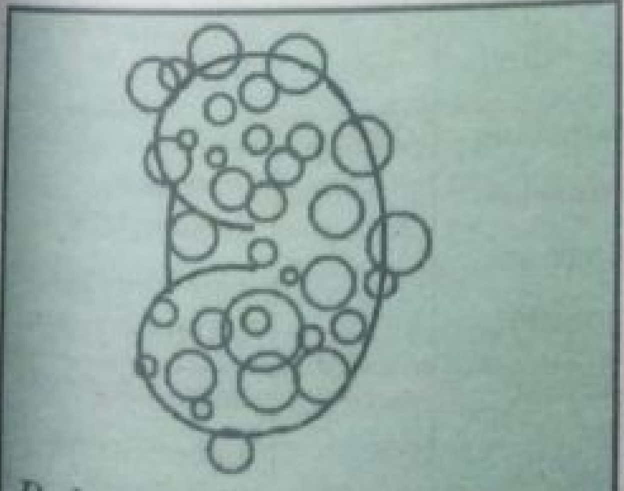
Dz	*Gene*	*Associations*
Polycystic Kidney Disease	ASD	SAH, Liver, Pancreas Hematuria, Flank Pain, Infxn, Stones, HTN Ultrasound or CT to see cysts
Polycystic Kidney Disease	ASR	Radially aligned cysts at birth Barely compatible with life (peds only)
Simple Cyst		Incidental finding do... nothing
Complex Cyst		Biopsy to rule out malignancy
Renal Cell Carcinoma		Smoking, ESRD, VHL Flank Pain, Flank Mass, Hematuria Ultrasound or CT scan to find it Needle to biopsy it Excision, Ø Rads / Chemo available Epo Paraneoplastic Syndrome or Anemia

CYSTS AND CANCER

Polycystic Kidney Disease

Scanned with CamScanner

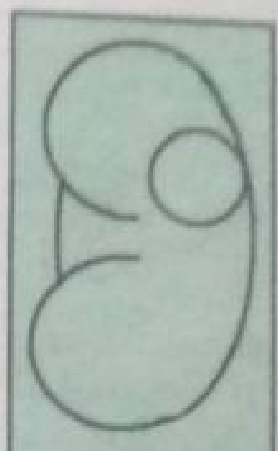
- A common disease in the population, it's responsible for **5-10% of ESRD** (end stage renal disease) and **Dialysis**.
- It's an **autosomal dominant** genetic disease that insidiously converts the renal parenchyma to cysts.
- These cysts have **no orientation** and can be any **size**.
- Eventually, functional nephrons are obliterated and replaced.
- Along the way the cysts can **bleed** (producing **pain** and **hematuria**, commonly mistaken for stones), get **infected** (pyelo), or actually form **stones**.
- These cysts also retain the ability to activate the **RAS** and can produce **malignant hypertension**.
- A symptomatic patient can be diagnosed with an **Ultrasound**. There's no treatment, but **manage complications** then do **dialysis / transplant** when they finally fail. What's critical in this disease is to identify the **Extrarenal manifestations**. Cysts can form in the **liver** (cirrhosis), **pancreas** (pancreatitis) and in the **cerebral vasculature**; they predispose the patient to **subarachnoid hemorrhage**.



Polycystic Kidney Disease

Simple Cysts

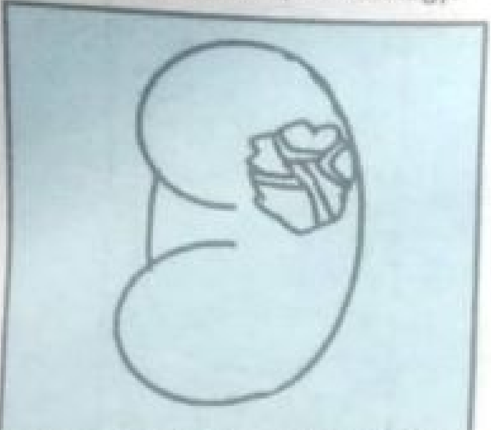
- Sometimes an ultrasound or CT will reveal a cyst.
- If it's simple - **no echoes** and just **one continuous mass** (like a smooth balloon) - there's no need to worry about it.
- If symptoms develop, **biopsy** and then **excise.**



Simple Cyst

Complex Cysts

- If that ultrasound or CT reveals a **large** or **septated** cyst it must be biopsied to **rule out malignancy**.
- Do a needle-guided biopsy and treat if it's a cancer or for symptomatology.



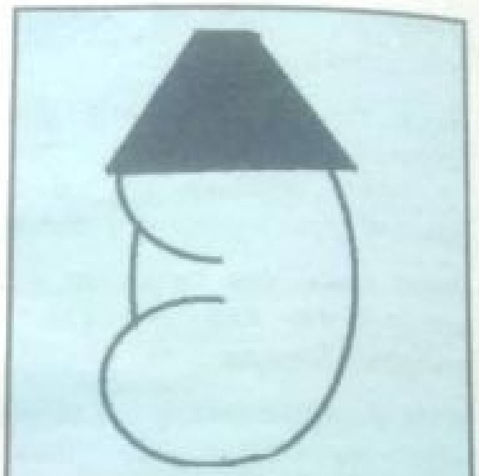
Septated Complex Cyst

Renal Cell Carcinoma

- A Renal Cell Carcinoma can be detected from the ultrasound or CT, which is why the biopsy's done for complex cysts.
- If the classic triad of **flank pain**, **hematuria**, and a **flank mass** is seen it's almost guaranteed to be cancer (though it may not always be present).
- Patients are at increased risk with **smoking**, **ESRD**, and with **Von Hippel-Lindau**.
- If a hematuria comes up on a U/A, go ahead and get an **ultrasound** or **CT** the flank to visualize the kidneys.
- **Biopsy** the lesions and **resect**.
- Since the renal cell carcinoma spreads **hematogenously** disseminated spread may have already occurred.
- **Renal vein thrombosis** is a real problem with this cancer. Finally, there can also be either **anemia** or **Polycythemia**.
- Either the cancer is stealing the blood (anemia) or it's actually producing an **epo paraneoplastic syndrome**.

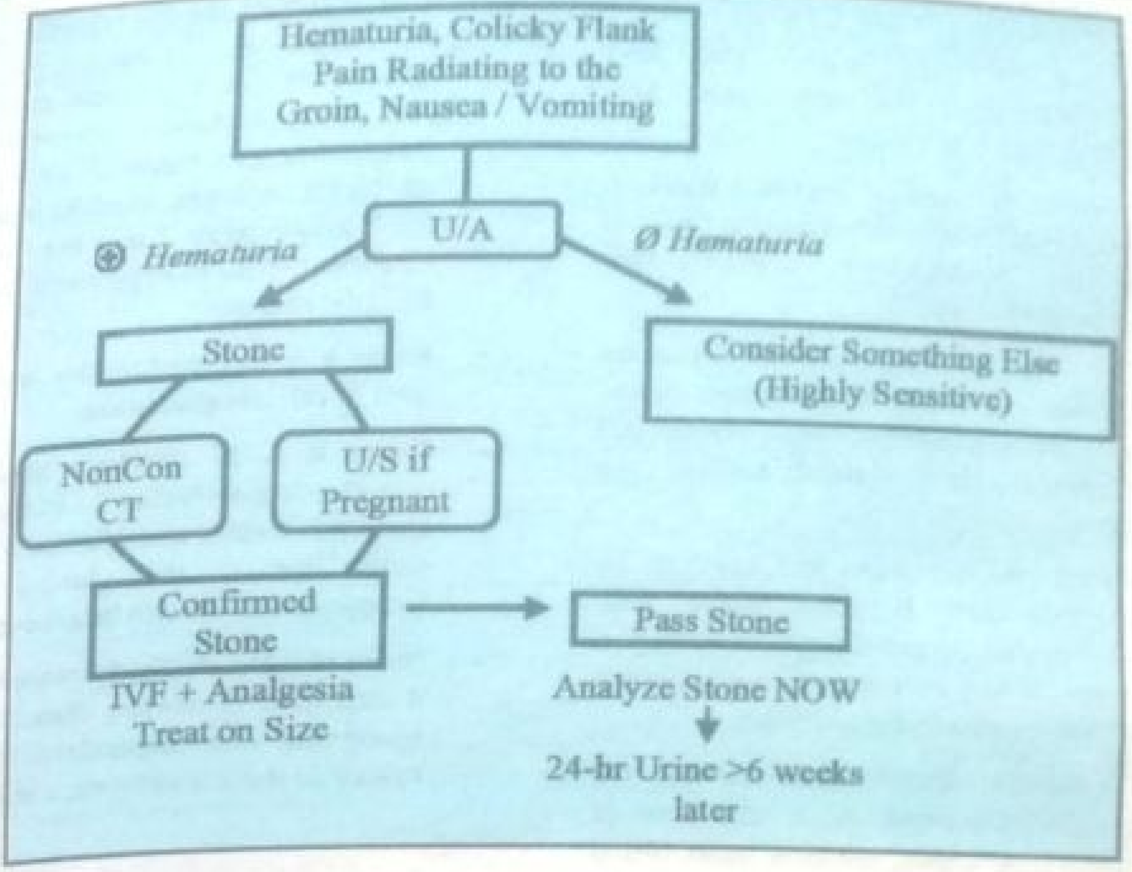
KIDNEY STONES

- Kidney stones come in a variety of forms. They're caused by the **precipitation** of something - either because their **quantity is large** or due to **decreased intravascular volume**. Each type has its own risk factor, which is why there needs to be a **close analysis** of both the stone and the urine after the stone passes.



Renal Cell Carcinoma

Types of Stones	***Radio-***	***Risk Factors***
Calcium Oxalate	Opaque	↑ Ca - Thiazide ↑ Oxalate - ↓ Meat in diet ↓ Citrate - ↑ Fruit in diet
Magnesium Ammonium Phosphate (Struvite)	Opaque	Alkaline Urine secondary to frequent UTIs with Urea-Splitting bacteria (Proteus)
Uric Acid	Lucent	Gout - Allopurinol Tumor Lysis - Rasburicase
Cysteine	Lucent	Rare inherited rental tubular defect


Hematuria, Colicky Flank Pain Radiating to the Groin, Nausea / Vomiting
U/A
⊕ Hematuria
Ø Hematuria
Stone
Consider Something Else (Highly Sensitive)
NonCon CT
U/S if Pregnant
Confirmed Stone
IVF + Analgesia
Treat on Size
Pass Stone
Analyze Stone NOW
24-hr Urine >6 weeks later

- The typical patient will present with **colicky flank pain** that **radiates to the groin** and **with nausea / vomiting**.
- This presentation may mimic pyelonephritis (look for a fever and white cell casts) and renal cell carcinoma (look for a palpable mass).
- Because of the similarities between diseases, start with a **urinalysis**. The **absence of casts** and the **presence of blood** (even microscopic hematuria counts) is indicative of the stone. In the absence of microscopic hematuria, the likelihood of a symptomatic stone is quite low.
- The diagnosis is confirmed with a **Non-contrasted CT scan** – by far the best test. There will be times where that test is not available, as in pregnancy. **If pregnant, use ultrasound**. While ultrasound may not be as sensitive for distal stones or hydroureter as CT, it can be done safely without exposing the fetus to radiation.
- **KUB** should **NOT** be used for diagnosis, but can be used to track disease progression in known stone disease. Intravenous Pyelogram is no longer used.

Path:	Precipitates form stone in tubules or ureters
Px:	Hematuria, Colicky Flank Pain that Radiates to the Groin, no fever or leukocytosis
Dx:	1st: U/A Best: Non-Con Scan Other: U/S if pregnant KUB if tracking disease IVP never
Tx:	<5mm: IVF + Analgesia <7mm: MET (CCB, Alpha Blocker) <1.5cm: Lithotripsy (proximal), ureteroscopy (distal) >1.5cm: Surgery Sepsis: Nephrostomy (proximal), Stent (distal)
F/U:	Strain and Analyze Stone 24-hr urine for Ca, PO4, Urate, Oxalate

lanagement is based on the size of the stone:

- If <5 mm the stone will **pass spontaneously**. Hydration and pain control is all that's needed.
- If <7 mm use **medical expulsive therapy**. This is achieved with Calcium Channel Blockers (Amlodipine), Alpha-Blockers (Terazosin) or both.
- **If <1.5 cm**, the stone is unlikely to pass on its own and needs to be broken down. Both **ureteroscopy** (for distal stones) and **lithotripsy** (for proximal stones) are appropriate.
- If >1.5 cm, the stone will need to be resected. This is done either with laparoscopic exploration (proximal stones) or with percutaneous anterograde nephrolithotomy (distal stones).
- If emergent, decompression of the GU system is required. As in the case of **obstructive sepsis**, either a **stent** (distal disease) or **nephrostomy** (proximal disease) is indicated.
- Regardless of the way the stone's taken out, it **needs to be analyzed.** Then, **6 weeks later** analyze a **24-hr urine**. Correct the risk factors and bam! good as new.

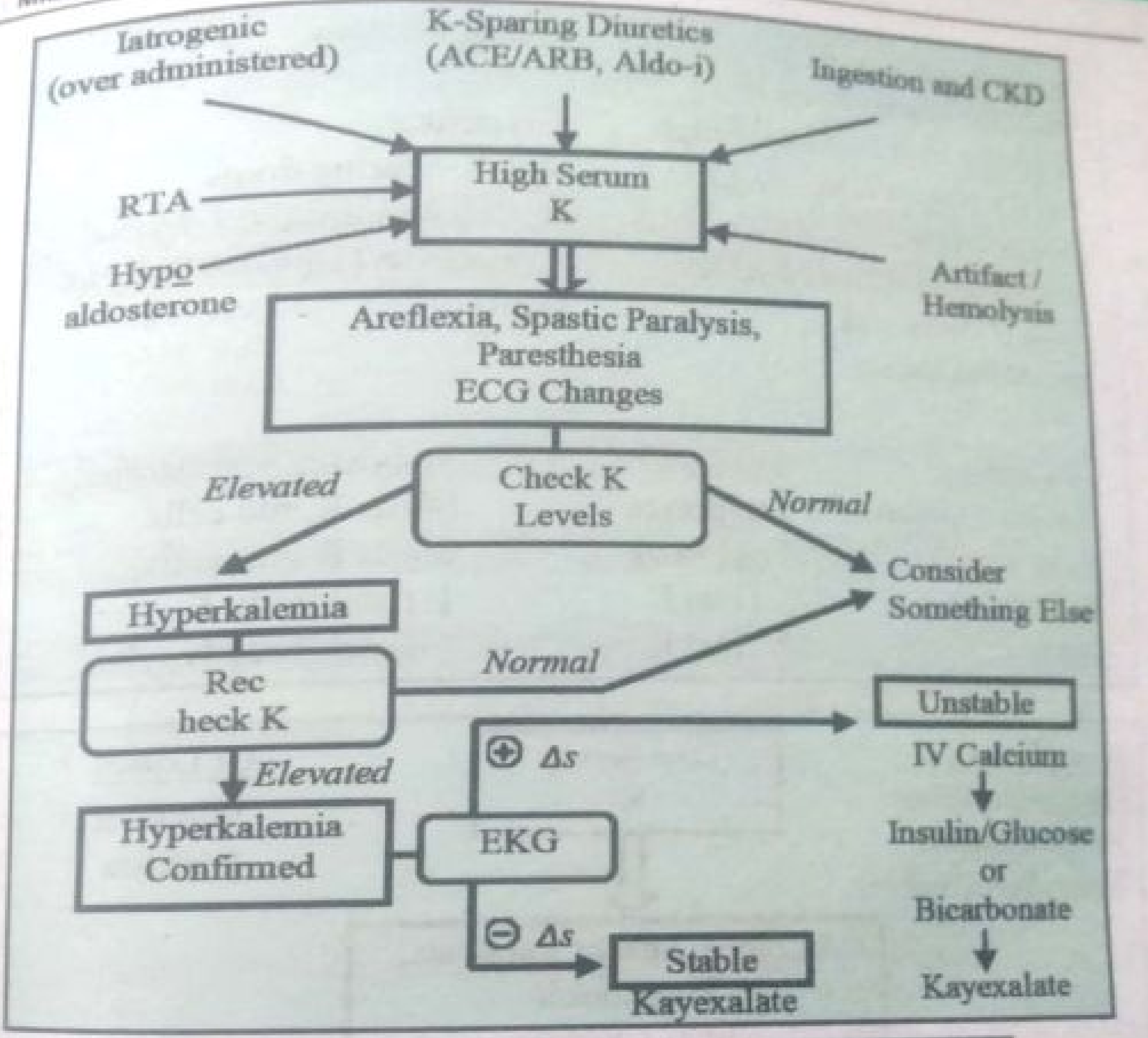
ISORDERS OF POTASSIUM

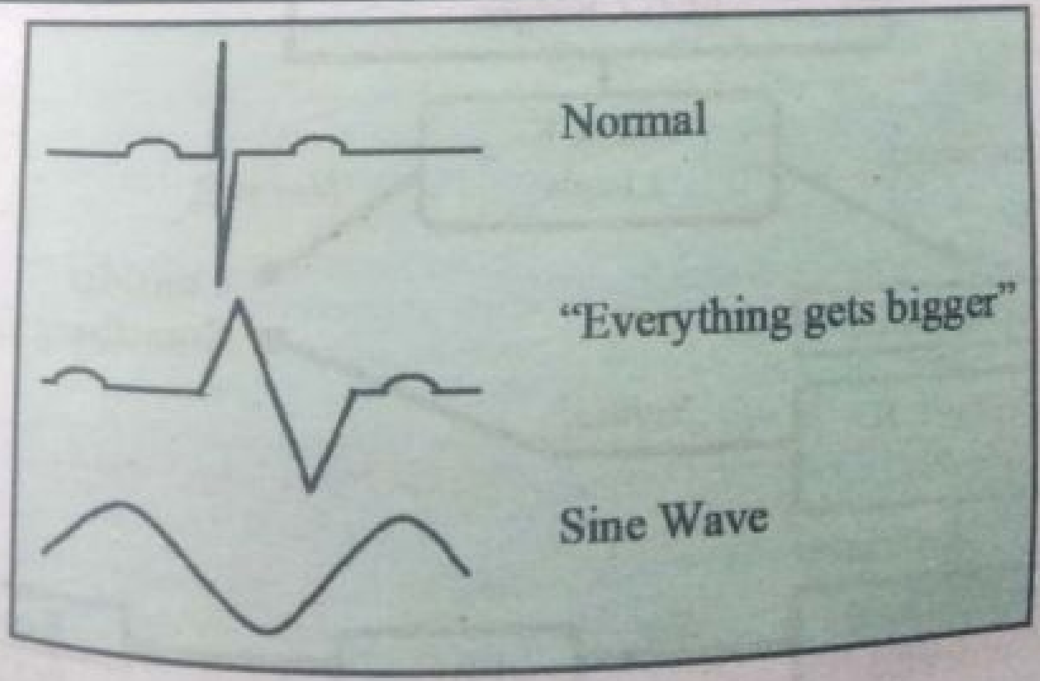
perkalemia

- Extracellular potassium is tightly regulated.
- It doesn't take that much extra potassium in a syringe to kill someone (**death penalty**).
- The range is typically **3.5 – 5.5** (>4.0 is normal in cardiac patients).
- There are many causes of hyperkalemia – some rare, some common.
- They all lead to the same symptoms: **areflexia, flaccid paralysis, paresthesia** (aka decrease motor and sensation) and **ECG Changes**. Whenever there's an abnormal potassium level, the first thing to do is **repeat the lab** (the sample could be busted or the cells could have hemolysed). Yet, the crucial evaluation is the **ECG 12-Lead**. Remember that "everything gets bigger..." as the **K goes** up the **PR prolongs**, the **QRS widens**, and the **T waves peak**. There are 3 phases of treatment. They're dependent on severity and ECG changes.
- **Phase I** is to stabilize the myocardium with **IV calcium gluconate**.
- **Phase II** is to **decrease serum K** by sequestering it - hiding it - in the cells. Do that with **Insulin and glucose** (the insulin shifts the K, the glucose prevents hypoglycemia) or with **Bicarbonate**.
- **Phase III** is to actually **decrease total body K** with either K-wasting **diuretics** or more commonly with **Kayexalate**. If in Renal Failure or the K is extreme, use **Dialysis**.

Hypokalemia

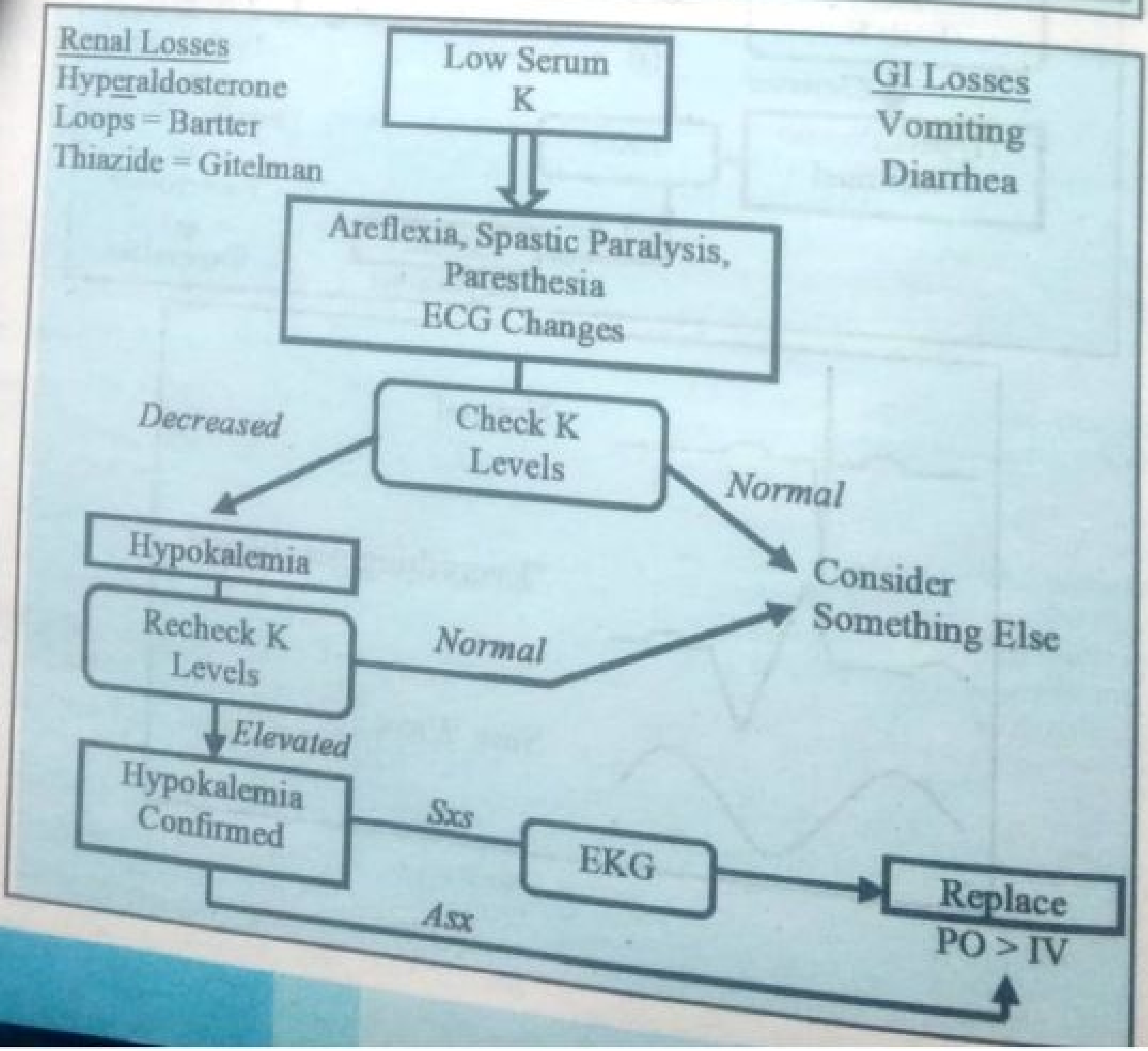
- Less exciting than hyperkalemia but just as deadly, a **low potassium** has multiple potential causes.
- It's usually going to be through either **GI losses** (diarrhea, laxatives, vomiting) or **Renal Losses** (hyperaldo states, loop diuretics or thiazide diuretics).
- While **rechecking the K** and **checking an EKG** could be done, mostly the K is simply repleted.
- Repletion is performed with oral or intravenous potassium. **Oral replacement is preferred**. If IV is to be used, the rate must be **<10mEq / hr** if by peripheral IV (PIV), or **<20mEq/hr** if by central line.


Iatrogenic
(over administered)
K-Sparing Diuretics
(ACE/ARB, Aldo-i)
Ingestion and CKD
RTA
High Serum
K
Hypo
aldosterone
Artifact /
Hemolysis
Areflexia, Spastic Paralysis,
Paresthesia
ECG Changes
Elevated
Check K
Levels
Normal
Consider
Something Else
Hyperkalemia
Normal
Rec
heck K
Unstable
⊕ Δs
IV Calcium
Elevated
Hyperkalemia
Confirmed
EKG
Insulin/Glucose
or
Bicarbonate
⊖ Δs
Stable
Kayexalate
Kayexalate


Normal
"Everything gets bigger"
Sine Wave

K comes back high on a lab draw	Repeat the draw
K comes back confirmed high but the patient is asx, Ø EKG Δ	Kayexalate, Stop K-Sparing drugs
Symptoms or EKG Δs With or without elevated K	IV Calcium, Insulin/Glucose, Kayexalate, Consider Dialysis
Renal Failure and any of the above	Dialysis

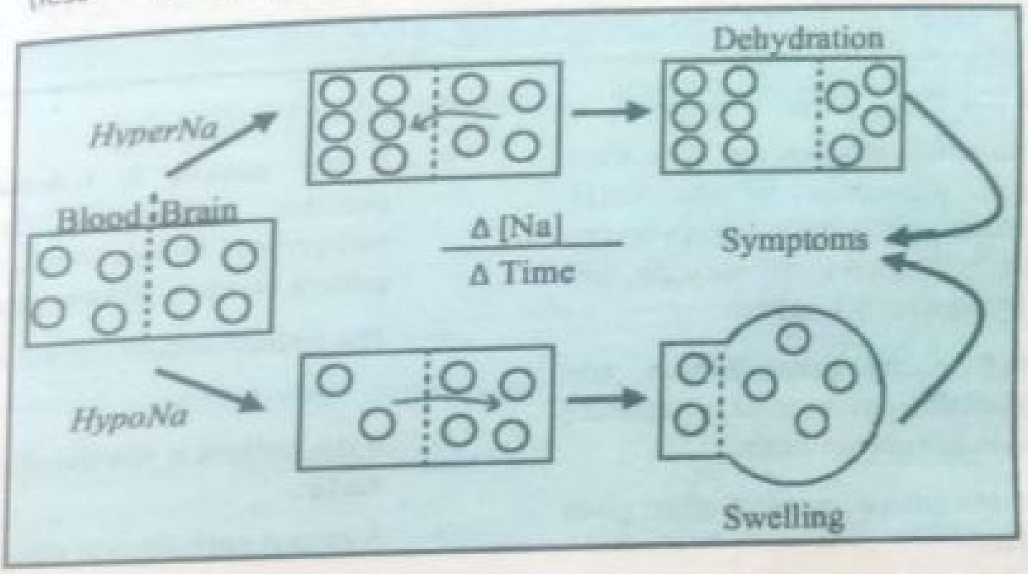
IV Calcium	Stabilize	Stabilizes Myocardium
Insulin + Glucose	Temporize	Shifts K into cells
Bicarbonate	Temporize	Shifts K into cells
Kayexalate	↓ Total K	↓ Total Body K
Dialysis	↓ Total K	↓ Total Body K


Renal Losses
Hyperaldosterone
Loops = Bartter
Thiazide = Gitelman
Low Serum K
GI Losses
Vomiting
Diarrhea
Areflexia, Spastic Paralysis, Paresthesia
ECG Changes
Decreased
Check K Levels
Normal
Hypokalemia
Consider Something Else
Recheck K Levels
Normal
Elevated
Hypokalemia Confirmed
Sxs
EKG
Replace
PO > IV
Asx

DISORDERS OF SODIUM

Introduction

- Disorders of sodium are really disorders of water balance.
- Normally, there are **two compartments - the blood and the brain**.
- These compartments are in equilibrium. If there's a disturbance in how much "stuff" is in the blood the water will shift. When there's too much "stuff" in the blood, water will move out of the cells and into the blood to balance it (**Hypernatremia**), **dehydrating** the cells. If there's too much water (less "stuff") in the blood (**hyponatremia**), the water will move out of the blood and into the cells to balance it, causing them to **swell**. Either way, that's bad news for the cells. It's the dehydrating and swelling that leads to symptoms.
- To fix **Hypernatremia** (which is always a deficiency in water) the task is easy. **PO Water** is always the best way to replace a water deficit. However, there may also be the need for **Hypotonic Solutions** such as D5W or 1/2NS. Before replacing the free water deficit, replace volume with Normal Saline.



- To fix **Hyponatremia** the task is a bit more challenging. If the patient is in a **severe state** (regardless of the diagnosis), use **Hypertonic Saline (3%)**. **If not severe,** then the management is based on the underlying diagnosis. **For example,** SIADH is treated with volume restriction, volume overload with diuresis, and volume depletion with volume resuscitation. To determine which course of action to take, further investigation is required.
- Sodium correction should occur **no faster than 0.25mmol/hr** unless severe. Correction by 4-6 is all that is required to eliminate symptoms in most cases. ***If sodium is corrected to quickly,*** it may result in **osmotic demyelination syndrome** (formerly called ***central pontine myelinolysis),*** leaving the patient a spastic quadriplegic. Thus, a **regular assessment of the Na** is required.

Isotonic Hyponatremia = Pseudohyponatremia

- Pseudohyponatremia is a product of laboratory artifact. The **calculated osmoles** will be elevated, but **measured** will be normal. This is a result of fats and proteins. Newer labs rarely encounter this issue.

Hypertonic Hyponatremia

- There can be other "stuff" in the blood that accounts for osmotic activity other than sodium.

- While the measured sodium is low, the **measured osmoles are elevated.**
- This is usually a product of **glucose**, **BUN**, or sugar alcohols.
- For every **100mg/dL** of glucose above 100 adjust for the Na by 1.6.
- If the corrected sodium is normal, correct the osmotic compound alone.

Onset	*Symptoms*	*Treatment*
Mild	Asymptomatic	HypoNa: Dz-Specific HyperNa: Po Water
Moderate	Nausea, Vomiting, Headache (all non-specific)	Hypo Na: IV NS HyperNa: IV NS NOT Hypertonic
Acute or Severe (Na<110, Hours)	Coma, Seizures, Death	HypoNa: IV Hypertonic HyperNa: IV D5W

ypotonic Hyponatremia = True Hyponatremia

- If the **measured osmoles** are low, then the original assessment of the water status was accurate. Now it's up to you to determine the underlying etiology and correct it to correct the sodium.
- Assessment of the **Urine Sodium** and **Urine Osmolality** can be used to separate most causes of hyponatremia.
- However, the clinical scenario often gives the answer.
- This is especially true on a vignette, where there can't be a mystery to have a single correct answer.
- If a urine sodium is decreased, the kidney is working and there's poor perfusion to it.
- If the urine osmoles are concentrated, ADH is activated.

Hypervolemic Hyponatremia

- If the patient is **wet** (i.e. JVD, edema, CHF, Anasarca), they're **overloaded**.
- The fluid is in the third space and needs to be mobilized.
- Treat with **diuretics**.

Hypovolemic Hyponatremia

- If the patient is **volume down** (dry mucous membranes, burns, fevers, tachypnea, hypotension), then all the patient needs is **Volume resuscitation**.
- The sodium should correct with IVF.

Euvolemic Hyponatremia

- If the patient is **euvolemic,** we're left with **RATS**.
- Rule out each disease one at a time.
- Renal Tubular Acidosis is assessed with a urinalysis, Addison's disease with cortisol, and Thyroid disease with a TSH.
- **SIADH** is a diagnosis of exclusion. It's treated with **volume restriction** and **gentle diuresis**. Refractory cases can be treated with **demeclocycline**. Check out the endocrine topics for details.

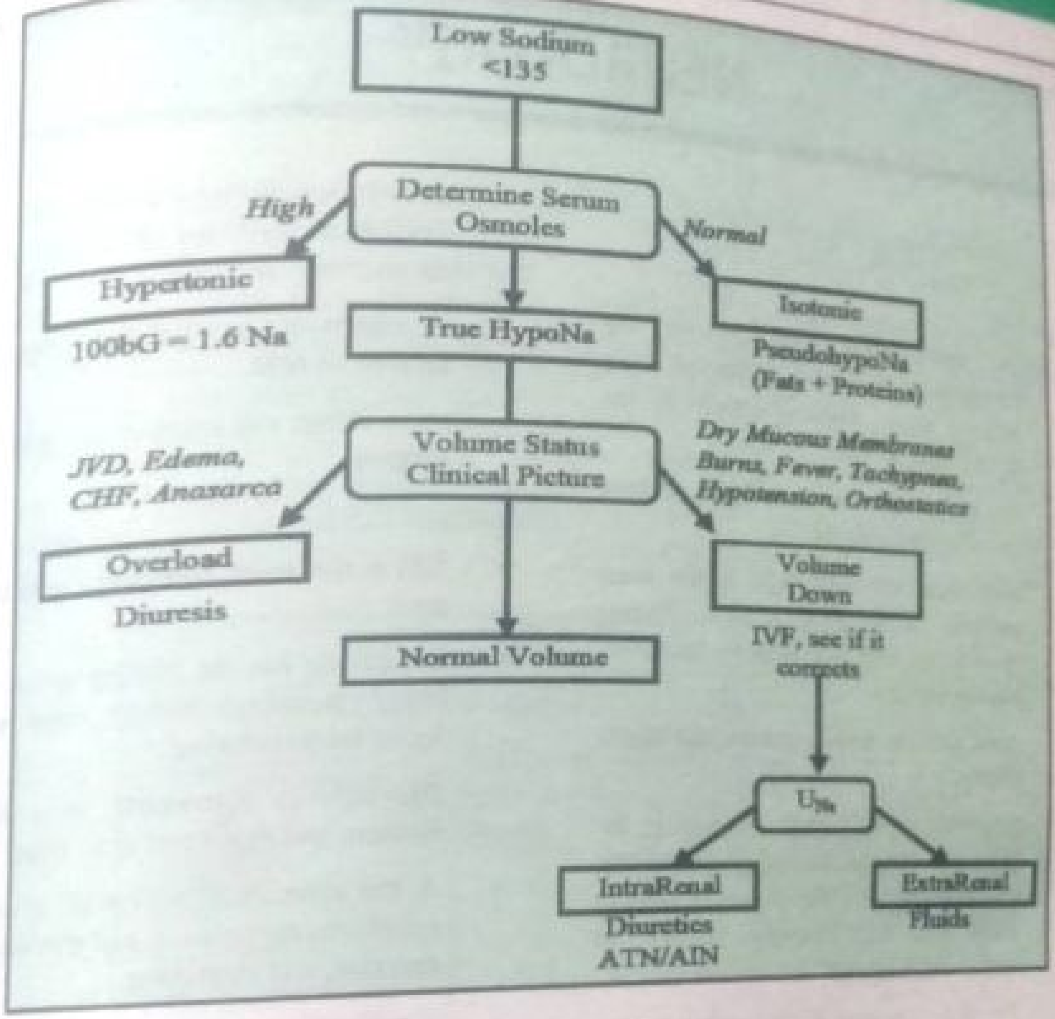
Vaptans

- Vaptans are absolutely contraindicated in hypovolemic hyponatremia.

Fluids

- Fluids are discussed in greater detail in the Intern content.

Volume resuscitation is done with Normal Saline or Lactated ringers; it's provided as a bolus.


Low Sodium
<135
Determine Serum Osmoles
High
Normal
Hypertonic
100bG = 1.6 Na
True HypoNa
Isotonic
PseudohypoNa
(Fats + Proteins)
Volume Status
Clinical Picture
JVD, Edema, CHF, Anasarca
Dry Mucous Membranes
Burns, Fever, Tachypnea,
Hypotension, Orthostatics
Overload
Diuresis
Normal Volume
Volume Down
IVF, see if it corrects
U$_{Na}$
IntraRenal
Diuretics
ATN/AIN
ExtraRenal
Fluids

Free Water is replaced with **hypotonic solutions**, given either as PO free water or D5W. ½ NS is a hypotonic solution and can be used to administer free water, but I want you to learn it as maintenance fluid.

Maintenance fluid is administered as any combination of ½ NS, ¼ NS, with or without D5.

Nutrition is provided as PPN or TPN. D5 containing solutions do not count.

$$\text{Serum Osmoles} = (2xNa) + \frac{\text{Glucose}}{18} + \frac{\text{BUN}}{2.8}$$

Volume	*Maintenance*	*Free Water*	*Nutrition*
NS	½ NS	PO Water	TPN
LR	½ NS D5	D5W	PPN
	¼ NS		
	¼ NS D5		

NEUROLOGY

BACK PAIN

ntroduction

- **The spinal cord runs through the vertebrae of the spine, protected from external injury.** Muscles attach to the **spine on the outside.**
- **Any disruption to muscle, bone**, or cord **can produce back pain.**
- **Since** musculoskeletal pain is the most common cause of back pain, finding reasons to look for deeper problems becomes critical.
- Most patients **do not require additional testing**.
- Diagnostic testing should be reserved for those with progressive neurologic deficits, failure to improve after 6 weeks, and in those who you strongly suspect an underlying diagnosis.
- The diagnostic step of choice often **begins with X-ray,** though the **MRI is always best**.
- A CT scan may be used in cases where the MRI is contraindicated (Pacemaker).

1. Cord Compression

- Irrespective of the underlying condition, any **warning symptoms** of cord compression warrant immediate investigation.
- This is a **neurologic emergency**.
- Intervention significantly improves morbidity (increased ambulation after treatment) - especially when started early.
- If any alarm symptoms are found the thing to give is **dexamethasone** (immediately).
- Since symptoms have already manifested themselves look for something big and obvious with an **X-ray**.
- If positive, it's positive. If negative, follow up with an **MRI**.
- Most things will respond to **radiation** or **surgery**.

2. Musculoskeletal

- This is the **most common** cause of back pain.
- It typically has an **inciting event** (heavy lifting, straining), though none may be found on questioning.
- The pain is **symmetric**, in a **belt-like fashion**, and described as an **ache**.
- In the absence of neurologic or systemic symptoms do nothing. Just give **analgesia**, **exercise**, and **stretching**.
- If symptoms do not improve, follow up with an **XR** then **MRI**.
- Give the patients 4-6 weeks before returning.
- It typically occurs in people **> 30**.

3. Herniation

- In the patient where musculoskeletal pain is being considered, one must **rule out herniated disk**.
- The age group and exacerbating factors are the same.
- However, people with herniation will have a **lightning** or **shooting pain** down the leg ("sciatica"), exacerbated by **hip flexion**, **movement**, **cough**, or **activity**.
- Assess **plantar flexion** (L4) and **Dorsiflexion** (L5), the common nerves impinged by a bulging disk.

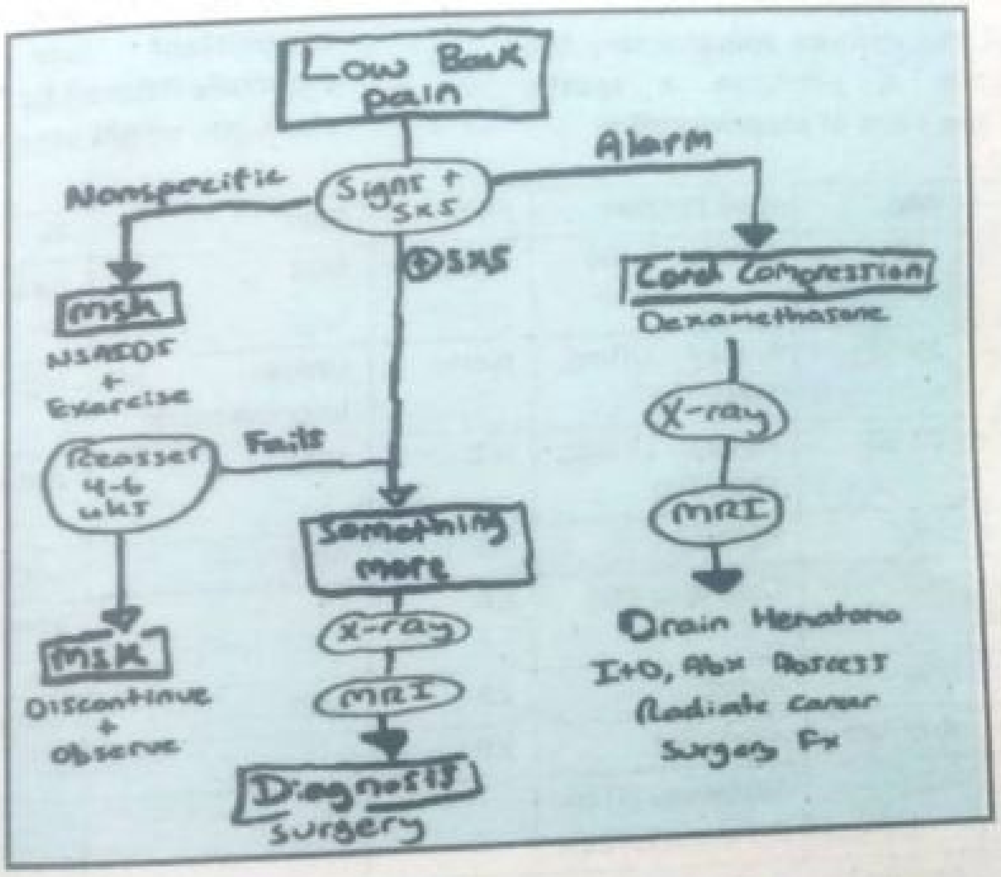
- Here's the deal: **neurosurgery** is better than conservative at 6 months, but they're the same at 1 year.

4. Osteophyte

- If you've found a patient that might have a herniation (they have that shooting lightning pain) but is an **elderly male** think osteophyte, a simple bone growth into the exit of the nerve route.
- Get an **XR** then **MRI** to rule out a compression fracture.
- Here, **neurosurgery** is better than waiting.

5. Compression Fracture

- In an **elderly patient** with back pain and a **history of osteoporosis** suspect a fracture.
- Do an **X-ray**, see the fracture, and get a neurosurgeon or orthopedist to fix it.
- There is usually **point tenderness** or a **vertebral step off** and warning symptoms may be present.
- These may occur with trauma, but only in the frail old ladies who fall on their butt (coccyx).


Low Back pain
Signs + Sxs
Nonspecific
Alarm
⊕ Sxs
MSK
NSAIDs + Exercise
Reassess 4-6 wks
Fails
Something more
X-ray
MRI
Diagnosis
Surgery
MSK
Discontinue + Observe
Cord Compression
Dexamethasone
X-ray
MRI
Drain Hematoma
I+D, Abx Abscess
Radiate Cancer
Surgery Fx

Warning Symptoms

- History of Cancer
- Urinary Symptoms (Incontinence or Retention)
- Sexual Dysfunction (ED or Priapism)
- Bilateral Lower Extremity Weakness
- Sensory Deficits in a Dermatome
- Fever

6. Spinal Stenosis

- Typically found in an **elderly patient** presenting with a unique form of **"sciatica."**
- There's often **leg and butt pain** that sounds like **claudication** but is positional (when upright with exercise symptoms, when hunched over symptoms).
- Do an **MRI** to confirm it and **Surgery** to fix it.

- From here on we can talk about other non-traumatic causes of neurologic symptoms or back pain. You can turn your eyes off if you're reading this for surgery.

7. Syringomyelia

- A pocket of CSF bulges into the anterior cord that produces back **pain** and **loss of pain/temperature sensation**, sparing proprioception.
- As it expands motor and sensation will be compromised. **MRI** diagnosis it, **surgery corrects** it.

8. Abdominal Aortic Aneurysm

- If a patient has a history of **HTN**, **CAD**, and **Smoking**, they might have an AAA.
- With AAA, the **anterior spinal artery** can be affected; it produces a **spastic paralysis** and a loss of **proprioception**.
- The back pain is from visceral compression (i.e. an aneurysm that is about to pop).
- It can be screened via an ultrasound.
- If there are neurologic symptoms it also requires an **MRI** and **Surgery**.

9. Visceral Organs

- Finally, visceral organs can **refer** to the back.
- In particular, **diarrhea/constipation** and **GYN** issues can cause back pain.
- Ask about neurologic symptoms.
- When negative, send them home on NSAIDs.
- If in the clinic and patients explain of **intermittent low back pressure**, especially relieved by flatulence or passing stool, you've got your answer.

	Age	*Risk Factors*	*First*	*Best*	*Tx*
Cord Compression	>50	Cancer, IVDA	Steroids	MRI	Dx Dependent
Musuloskeletal	20-50	Heavy Lifting, Straining	None	Unless no Improvement	NSAIDs
Herniation	20-50	Heavy Lifting, Straining	XR	MRI	Bed Rest, NSAIDs
Ostophyte	>50	Aging	XR	MRI	Surgery
Compression Fx	>50	Osteoporosis	XR	∅	Surgery
Spinal Stenosis	>50	Aging	XR	MRI	Surgery
Visceral Organs	Any Age	Anything	XR	-	-
AAA	>50	Smoking HTN< Atherosclerosis	-	-	-
Syrinx	Any Age	Trauma		-	-

COMA

ntroduction

- Producing **unconsciousness** - a depression of brain function that extends beyond executive function - requires significant CNS compromise.
- In each of the conditions we're going to discuss the patient is mostly **unaware** and **unable to be aroused**.
- The degree of arousal (response to external stimuli, brainstem function) determines what the diagnosis is.
- **Cerebral function** is the most sophisticated, the most human, and the least required for survival, so is sacrificed first, meaning that relatively **small insults** can induce **coma**.

- **Brainstem function** is vital and can persist despite the absence of awareness (breathing, sleep/wake cycles), leaving the patient in a **persistent vegetative state**.
- In the absence of cerebral function and brainstem function there's nothing left -- **brain death**.
- Watch out for **locked-in** syndrome which can look like any of the above, but the person is still fully alive, awake, and alert.

Coma

- Coma is a state of unconsciousness of **depressed cerebral function** such that there is **no response** to **internal or external stimuli**.
- Literally anything can produce coma: **Toxins** (EtOH, Benzos, Opiates), **Electrolytes** (all), and **Endocrine** (Hypothyroid, Thiamine) are potential reversible causes.
- However, to knock out all arousal there must be significant/catastrophic cerebral damage.
- It can occur via **hypoxic/ischemic encephalopathy** (drowning, cardiac arrest), trauma (**diffuse axonal injury**) or **brainstem path** (hemorrhage or infarction).
- By definition, coma is reversible.
- Do a comprehensive workup (**CMP, CT scan, LP, EEG**), give the **coma cocktail** (Thiamine, D50, Oxygen, Naloxone), and reverse underlying causes.
- A full recovery from comas is possible.

Persistent Vegetative State

- The patient has a **flat EEG** but **opens her eyes** or has a **positive caloric test**.
- The patient has no arousal but can move, display pain, and have sleep wake cycles.
- Nonetheless, the personality is gone; they're in a **persistent vegetative state**.
- They'll never recover and will require tube feeds/institutionalized care for life.

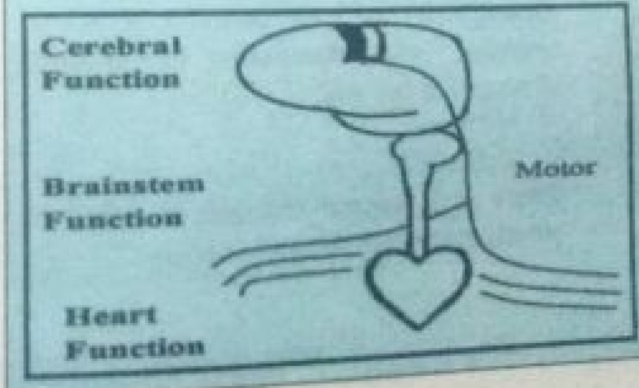
Brain Death

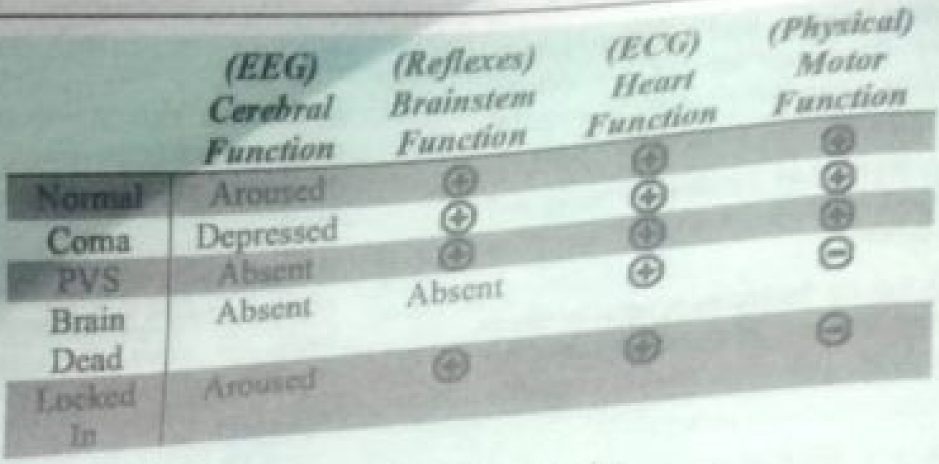
- If someone goes down and stays out despite resuscitative efforts, and attempts at reversal fail you must consider brain death.
- In brain death the **cerebral EEG** shows nothing: there's **no arousal, sleep wake cycle**, or **drive to breathe** (life is ventilatory dependent).
- Before confirming brain death rule out intact neural reflexes with a **caloric test** (COWS) and a **corneal reflex**.
- If there's no response brain death is in place and the patient should be removed from life support.
- **Two** doctors must confirm death.

Locked-In Syndrome

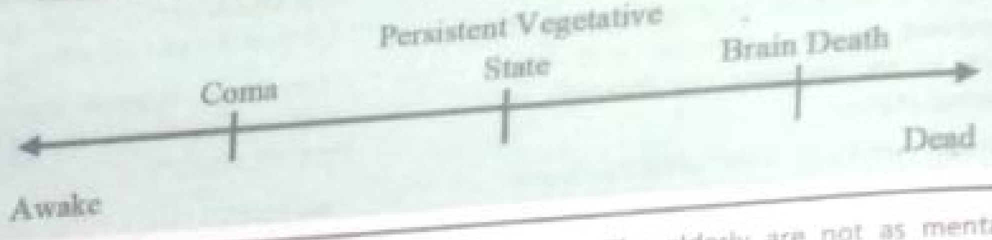
- The pons is the site where both **motor and sensory tracts** pass.
- If there's a **basilar artery infarct** or **central pontine myelinolysis** these tracts are severed.
- The patient LOOKS LIKE they're in a Persistent Vegetative State but they have **full awareness**.
- They're able to communicate via **eye movements**.
- There's no recovery from this. **MRI** should confirm the diagnosis; make the patient comfortable.

(1) True Coma
(2) Persistent Vegetative State
(3) Brain Death
(4) Locked-in-Syndrome





	(EEG) Cerebral Function	(Reflexes) Brainstem Function	(ECG) Heart Function	(Physical) Motor Function
Normal	Aroused	⊕	⊕	⊕
Coma	Depressed	⊕	⊕	⊕
PVS	Absent	⊕	⊕	⊕
Brain Dead	Absent	Absent	⊕	⊖
Locked In	Aroused	⊕	⊕	⊖



DEMENTIA

Introduction

- Dementia is about impaired cognition.
- Cognition is a complex combination of neuropsychological domains: memory, attention, executive function, language, social graces, and sensory motor abilities.
- Dementia is **not amnesia,** which is an acute loss of memory in an otherwise unimpaired individual.
- Dementia is **not delirium,** which has an impaired cognitive function + may even include memory loss, but is acute and the product of an underlying stressor. One of the key means of separating dementia from delirium is the timing: dementia is chronic, insidious, and doesn't change throughout the day. Delirium is acute, obvious, and fluctuates in severity throughout the day.

Spectrum

- There is a **normal changes of aging** in which minor forgetfulness occurs.
- The elderly are not as mentally nimble, have trouble learning new things, and may be forgetful.
- Choose normal changes of aging when there is forgetfulness without impairment in their life. Language comprehension and vocabulary are always preserved in normal aging, and neuropsychiatric testing is normal.
- **Mild Cognitive impairment** is "not dementia yet." This is where the line between normal aging and dementia blurs. It goes something like this: they have dementia, but it isn't bad enough to matter. They will have impairment on testing, less independence, but are able to still keep up appearances.
- **Dementia** is where there is significant functional deficit that compromises independence. Be looking for low scores on neuropsychiatric testing; there's often severe social or memory impairment.

Dementia Workup

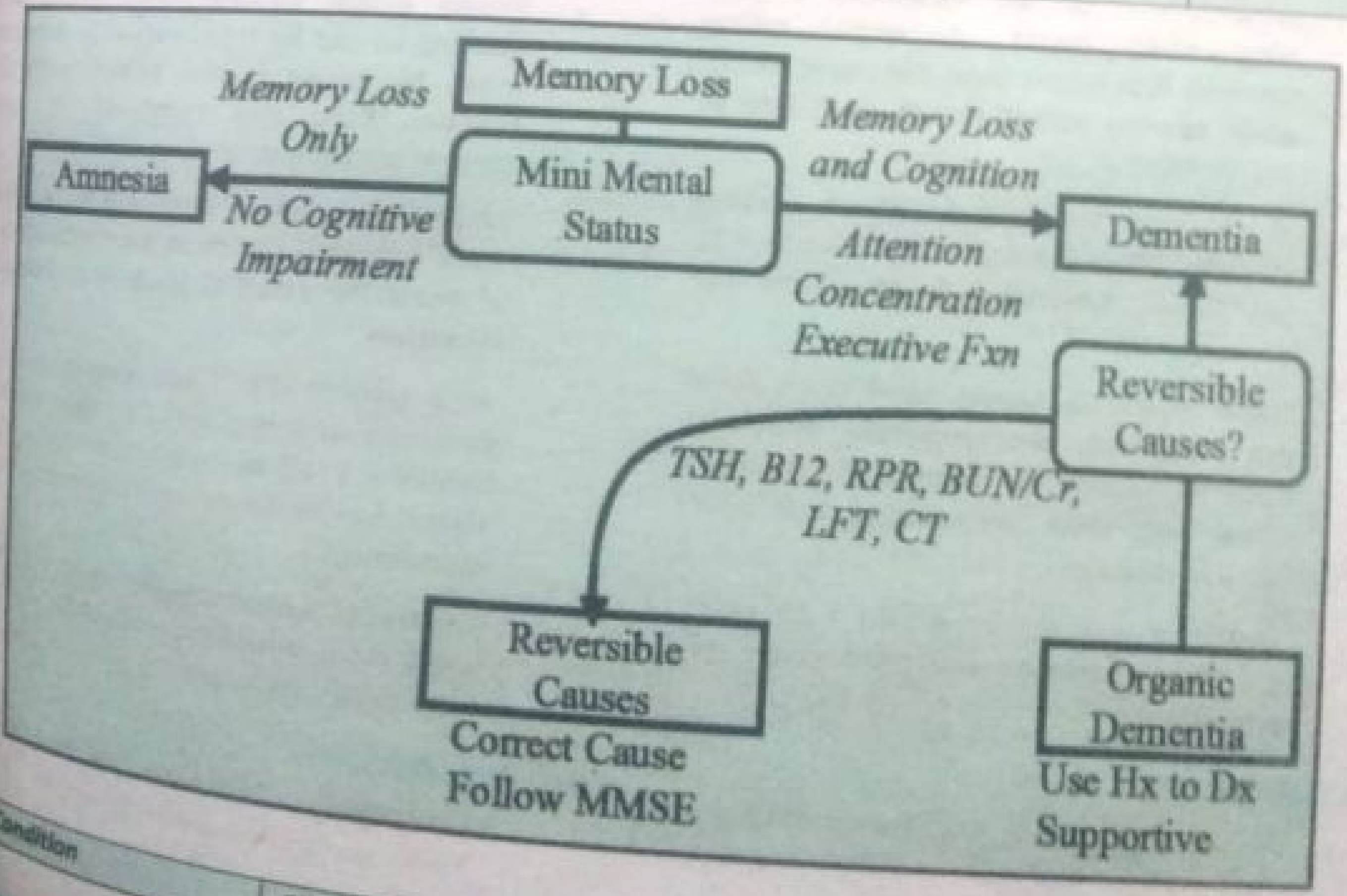
- Do not screen for dementia.
- It's usually a family member who notices impairment in cognition, memory, or social graces. One this is identified, some

neuropsychiatric testing should be performed to assess for impairment. The **mini-mental status exam** (< 22 of 30) or the **Mini-Cog** exam can be used.

- Once dementia is suspected, routine laboratories are obtained to rule out **reversible causes** of dementia, or those that mimic dementia. Assess CBC, LFT, Thyroid, BMP, and **Vitamin B12.** Correct abnormalities. **RPR** can be obtained in high-risk populations to rule out Neurosyphilis.
- **Depression** should be screened for and treated. Dementia in this setting is called **pseudodementia,** and occurs often around the time of the loss of a spouse.
- Brain imaging, either **CT scan** (cheaper, easier) or **MRI** (better for Creutzfeldt-Jakob disease and infections) is obtained. This can show evidence of **chronic subdural hematoma,** hydrocephalus, degenerative changes, and infarcts.

Dementia	Chronic, Insidious Cognitive impairment Memory loss only
Amnesia	Memory loss only Acute
Delirium	Acute, Overt Cognitive impairment Memory loss

Normal changes of Aging	***Mild Cognitive Impairment***	***Dementia***
Forgetfulness without cognitive impairment Language and vocabulary always retained	They have dementia but it isn't bad enough to impair them in society or independence	Significant loss of cognition, executive function, social graces, or memory


Memory Loss
Memory Loss Only
Amnesia
No Cognitive Impairment
Mini Mental Status
Memory Loss and Cognition
Dementia
Attention
Concentration
Executive Fxn
Reversible Causes?
TSH, B12, RPR, BUN/Cr, LFT, CT
Reversible Causes
Correct Cause
Follow MMSE
Organic Dementia
Use Hx to Dx
Supportive

Condition	***Clinical Picture***	***Test***	***Treatment***

Hypothyroid	Weight Gain, Heat Intolerance, Constipation, Malaise, ↓DTRs	TSH	Synthroid
B12 Def	Megaloblastic Anemia and Neuro sxs	B12	B12
Subdural Hematoma	Focal Neurologic Deficit, Headache, Trauma	CT	Surgery
Syphilis	Sexually Active, Any Neuro, Screen endemic areas	RPR	Penicillin
Uremia	Renal Failure, Uremic Frost	Cr	Dialysis
Cirrhosis	Asterixis, Ascites, Hepatomegaly	NH_4	Transplant Lactulose
Pseudo-dementia	Depression, Loss of Loved One	Psych	SSRI

Alzheimer's Disease (AD)

- This is the **most common** cause of organic dementia. Linked with **neurofibrillary tangles, neurotic plaques,** and **amyloid deposition**, a definitive diagnosis is only made on brain biopsy at **autopsy**.
- However, AD has a very classic presentation of an **insidious** (slowly progressive) onset dementia taking **memory first** (short term then long term), while **sparing social graces** until late in the disease.
- A CT scan will show **diffuse cortical atrophy**. There is a link to chromosome 21 (all **Down syndrome > 40 years old** develop AD).
- Once reversible causes have been ruled out treat with **cholinesterase inhibitors** such as tacrine or **donepezil (Aricept)**. These will **slow progression** but don't reverse disease.
- Death usually occurs within 5-10 years; it's often from a secondary cause like pneumonia.

ick's Disease

- In contrast to AD, the **Personality goes first** in Pick's disease.
- Social graces are lost (violence, hypersexual) but **memory remains intact**. Whereas AD has diffuse cortical atrophy, Pick's has **frontal** and **hypothalamic** degeneration.
- Diagnosis is clinical and there's no treatment.

CJD

- This disease is caused by an abnormal protein called a **prion**.
- Prions evade denaturation even with cooking so can be transmitted in infected meat, by eating human brains with the disease (Kuru and zombies), or with corneal transplant.
- While eating infected meat is certainly a scary thought, the most common means of acquiring prion disease is a **sporadic mutation.**
- In a patient that's **too young** to have dementia and displaying a **rapid decline** (within a year) of memory, consider CJD. There may be the associated symptoms of **myoclonus**.
- Treatment is palliative and death occurs in years from infection but usually months from diagnosis.

Lewy Body Dementia

- **Lewy-Body Dementia** is effectively Parkinson's disease with dementia.

- The two differ only by the time of onset and the pathology is the same (Lewy Bodies).
- Look for **Parkinsonian symptoms** and **dementia**

Multi-Infarct Dementia (Vascular)

- When someone has a stroke their memory and cognitive function may become impaired.
- The problem is a person with Alzheimer's Disease often has Risk Factors for stroke (**HTN**, **DM**, **CVA**), but without a focal neurologic deficit the stroke may not be diagnosed.
- However, if a patient has a stroke and gets **abruptly demented** or **abruptly worse** and you can tie the stroke temporally to the decline in cognitive function, call it vascular dementia (Multi-Infarct Dementia).
- An **MRI** may show old infracts, but these may be coincidental rather than causative. If there's a question treat it as Alzheimer's but of course control risk factors for stroke.

Normal Pressure Hydrocephalus

- This is both an **organic** and **reversible** cause of dementia.
- In an elderly patient with an **ataxic gait**, **urinary incontinence**, and **dementia**, get a CT or **MRI** to evaluate for hydrocephalus.
- The pressures are normal so there are no signs and symptoms of ↑ ICP.
- Since it's ↑ CSF causing the problem, it's possible to do **serial LPs** to take off extra fluid (if it improves it's also diagnostic) and eventually fit them for a **VP Shunt**.
- Be carefully calling cortical atrophy with subsequent volume expansion ***"Normal Pressure Hydrocephalus" (NPH is a specific diagnosis with specific criteria)***.
- Look for the person who is **wet** (urinary incontinence), **wobbly** (ataxia) and **weird** (dementia).

	Hitory	*Location*	*Diagnosis*	*Treatment*
Alzheimer's	Short Term Memory, Long Term Memory, then Social Graces, Chronic & Insidious Dz	Diffuse Cortical Atrophy	CT	Donepezil
Pick's Disease	Personality 1st Memory Later	Frontal-Temporal Degeneration	CT to r/o Clinical Diagnosis	None
CJD	Myoclonus Rapid Decline	Diffuse Cortical Atrophy	Clinical Diagnosis	None
Lewy Body	Delirium	N/A	Lewy Bodies on Stain	Donepezil maybe None
Multi-Infarct	Acute exacerbation with CVA	Anywhere	Clinical Correlation of dementia with CVA	Control CVA risk
Normal Pressure Hydrocephalus	Ataxic Gait, Urinary Incontinence Dementia	Nowhere	LPs Dx and Tx	Serial LPs, VP Shunt

DIZZINESS

Introduction

- "Dizzy" is a very vague complaint that needs further investigation.
- The first question needs to be what does the patient mean: **presyncope** or **vertigo**?
- In **presyncope** the patient will complain of blacking out, lightheadedness, or cardiac symptoms.
- In **vertigo** a patient will sense movement where none exists.
- This will present as either the **room spinning** or being **unsteady on their feet**.
- Once vertigo is established it's critical to differentiate between **central** (usually a structural lesion requiring **MRI** of the **posterior fossa**) and **peripheral** (sparing the need for costly MRI, focusing more on **symptom control**).
- Lesions that are **central** are generally **chronic and progressive**; they occur in the posterior fossa (i.e. away from ears, sparing aural symptoms) where the cranial nerves are.
- This produces **cranial nerve deficits**.
- Get an MRI and correct as needed.
- **Peripheral** lesions are essentially **in the ear**, away from cranial nerves, but **acute with ear symptoms** (hearing loss and tinnitus).

Posterior Fossa Lesions

- Whether it's **vertebrobasilar insufficiency** or a **posterior fossa tumor**, the main problem is a structural lesion compressing on or eating away at the **cerebellum** and **brainstem**.
- If there are **focal neurologic deficits** and **vertigo** it's almost pathognomonic for a central lesion.
- Get an **MRI**. If normal, follow with **MRA**.

Benign Paroxysmal Positional Vertigo

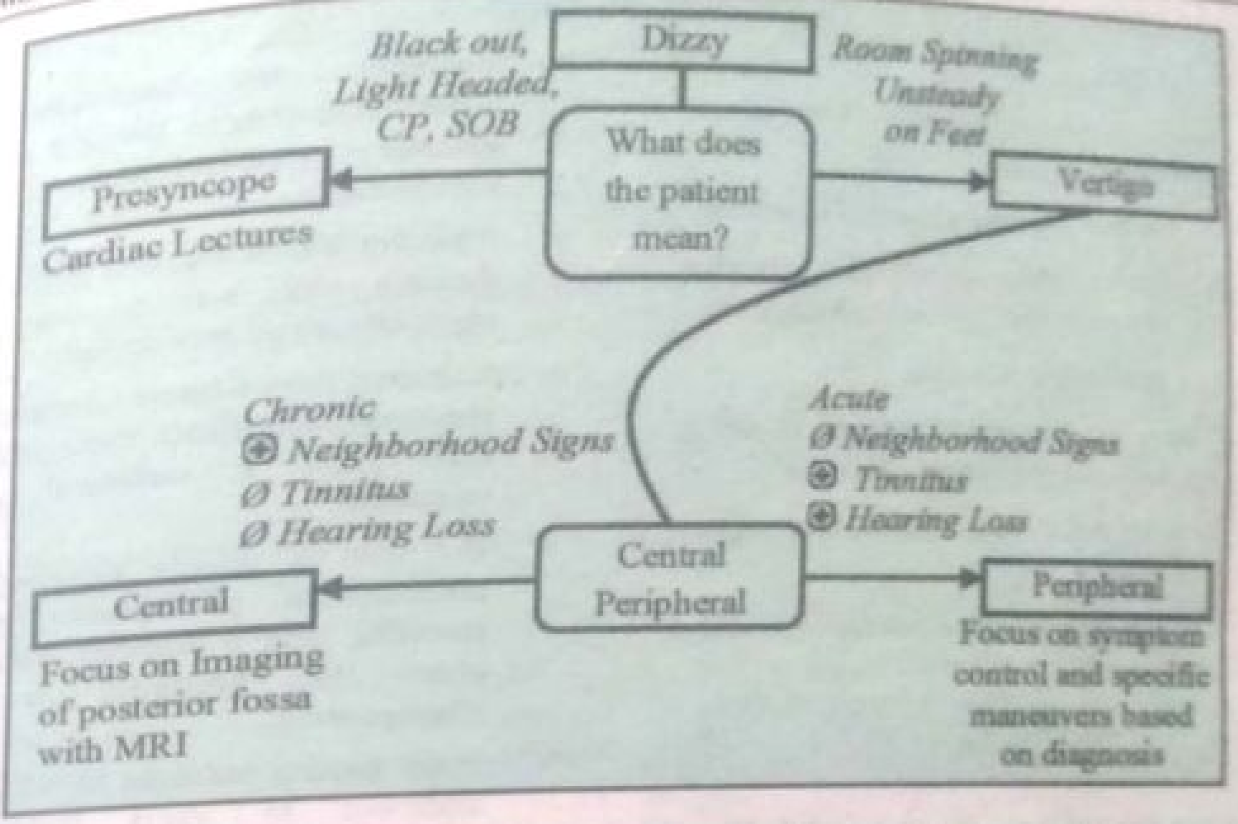
- This disease is caused by an **otolith** within the semicircular **canals**.
- It moves with **head movements** and settles randomly producing **vertigo** and **rotary nystagmus** on **head movement** that's **transient** (<1 minute).
- This occurs every time the head moves (easily reproducible). Sensation can be reproduced by the **Dix-Hallpike** maneuver.
- **Movement Exercises** dislodge and break up the stone, curing the patient of disease.
- An **Epley Maneuver** can be done in the office and is often curative.

Labyrinthitis/Vestibular Neuritis

- A diagnosis of exclusion.
- Suspect this disease in a patient with **vertigo**, **Nausea/Vomiting**, and **hearing symptoms** four **weeks after a URI** (pharyngitis, otitis, sinusitis).
- It's a diagnosis of exclusion because pontine strokes and tumors mimic the chronic nature of vertigo and the URI often goes unnoticed.
- If diagnosed early give **steroids** within 72 hrs.
- The disease will resolve in months, but balance and hearing may be compromised for those months.
- **Meclizine** can get them through the vertigo episodes.

Meniere's Disease

- A peripheral cause of vertigo presenting with a triad of **vertigo,** and **hearing loss, fullness,** or **tinnitus** that's **unrelated to movement**.
- Like BPPV, it's acute but the vertigo persists – lasting **~30 minutes**.
- This also occurs repeatedly, but not every time the head moves; it may be separated by long periods of time.
- Treat with **diuretics** and **low salt diet**.


Dizzy
Black out, Light Headed, CP, SOB
Room Spinning Unsteady on Feet
What does the patient mean?
Presyncope
Cardiac Lectures
Vertigo
Chronic
⊕ Neighborhood Signs
Ø Tinnitus
Ø Hearing Loss
Acute
Ø Neighborhood Signs
⊕ Tinnitus
⊕ Hearing Loss
Central Peripheral
Central
Focus on Imaging of posterior fossa with MRI
Peripheral
Focus on symptom control and specific maneuvers based on diagnosis

Disease	*Onset*	*Duration*	*Diagnosis*	*Treatment*
BPPV	With Movement, Acute, Reproducible	<1 min	Dix-Hallpike Rotary Nystagmus	Movement Exercise
Meniere's	Without Movement, Acute, Repetitive	30 mins	Clinical	Diuretic and Low Salt
Labyrinthitis	4 weeks after an URI, N/V, vertigo, deafness	Persistent, sxs may occur on and off for months	Diagnosis of Exclusion	Steroids.. Meclizine
Posterior Fossa Lesions	Chronic and Progressive	Persistent	MRI	Surgery Steroids CVA control

HEADACHE

Introduction

- One must be able to separate a **primary headache** which can be diagnosed mainly on the history and physical alone from a **secondary headache** which requires rapid investigation with imaging and invasive testing.
- Look for **red flags**.

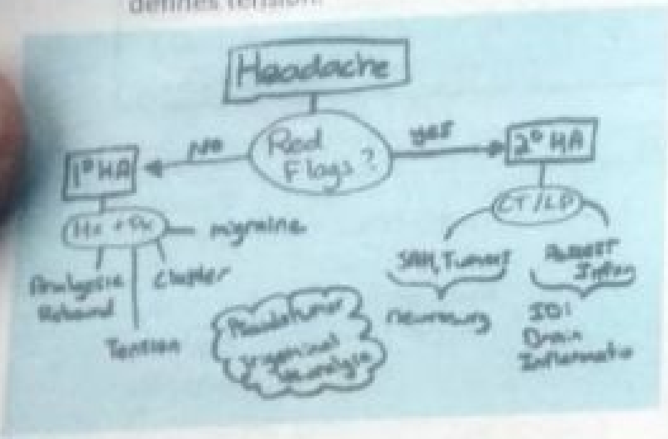
Red Flags

- **New Headache > 50**
- **Sudden Crescendo Headache**
- **Fever + Headache**
- **Focal neurologic deficits**

Primary Headaches

Tension Headaches

- This is a regular headache that you get from time to time.
- It's the **most common** cause of headache.
- It's usually **bilateral, vice-like** pain that radiates from the front to the **back/neck**.
- It' aggravated by exercise.
- There should be **NO** nausea/vomiting, photophobia or phonophobia.
- Treatment is usually with **acetaminophen** or **NSAIDs**.
- The absence of other headache features defines tension.



Cluster

- This is the ***most common "trigeminal autonomic cephalgia"***.
- It's characterized by **severe unilateral** pain that has **autonomic symptoms** (rhinorrhea, lacrimation, conjunctival injection, Horner's).
- Clusters of headaches occur in periods of **weeks** and are often **symptom free for months** (attacks "cluster" together).
- When cluster headache is diagnosed, an **MRI should be obtained** to rule out other diseases that mimic Cluster.
- **Oxygen** is **first-line** treatment and is often sufficient to abort attacks.
- **Sumatriptan** can be used if oxygen fails.
- Prophylaxis is with **calcium channel blockers** such as **verapamil**.

Migraines

- Migraines are generally poorly understood; they're thought to have a **vascular pathogenesis** (arterial vasodilation).
- A patient with a migraine may present in multiple ways with no one symptom especially sensitive or specific.
- Migraines have **triggers** (nitrites, caffeine, chocolate, menstrual cycle, stress, etc) that incite a **unilateral pounding headache**.
- The pain is usually **disabling** causing phonophobia, **photophobia**, **nausea / vomiting**, and a lingering malaise even after the headache is aborted (**"hangover"**).
- If the patient manages to fall asleep it's sufficient to abort the migraine, otherwise, the pain may last for **4-72 hrs** without intervention.
- For an ***active dynamic migraine*** decide if it's **mild** (use NSAIDs) or **severe**.
- ***If severe,*** initiate therapy immediately (early intervention decreases the need for back up medications).
- Start with a **Triptan** or an **Ergot** (**caution** if **CAD** as these drugs cause vasospasm).
- For a patient that has chronic migraines use cognitive feedback, trigger avoidance, and **prophylax** with **Beta Blockers (propranolol is best)**, Calcium Channel Blockers (verapamil or diltiazem), or Anticonvulsants (valproic acid, topiramate).

POUND Mnemonic for Migraines
- **P Pulsatile**
- **O One day in duration**
- **U Unilateral**
- **N Nausea and Vomiting**
- **D Disabling**

(Any 3 is diagnostic)

Analgesic Rebound

- Analgesic rebound can be any type of pain that occurs in a patient on chronic analgesics (**opiates, ergots, triptans, OTC,** taken **2-3 times / week**) who suffers from frequent headaches (**10x/month**).
- Withdrawing the offending medication may initially make the headaches worse, but this is simply a withdrawal symptom it'll pass if drugs are withheld.

Secondary Headaches

- Red flags and alarm symptoms are unique for each diagnosis. Knowing what test to do for which scenario is critical.
- The first step is to identify the alarm symptom. Follow it with the confirmatory test. These are discussed elsewhere in the course.
    - For **meningitis** look for **fever and a headache**. Do an **LP** with **Cx**, give Abx (CT?).
    - For **abscess** look for **fever, headache,** and **Focal neurologic Defect**. Do a **CT** scan then **drain**, give Abx.
    - For **tumor** look for a **progressively worsening headache worse in the AM**. Do a **CT / Bx**, give **Radiation / Chemo / Surgery**.
    - For **SAH** look for a patient with a **sudden onset** headache that's the **worst headache of their life**. Do a **CT**, get **Neurosurgery, control BP** and **HTN**.

Patient	*Presumed Diagnosis*	*Test*	*Tx*
Fever + Headache	Meningitis	LP	Ceftriaxone
Fever + Headache + FND	Abscess	CT	Drain, Abx
Worse in the morning and with cough or progressively worsening	Tumor	CT	Rads/Chemo
1st Time New Severe Headache	-	CT	-
Worst headache of their life or thunderclap headache	SAH	CT	Surgery

Idiopathic Intracranial Hypertension

- IIH is also called pseudotumor cerebri.
- It is **pseudo-tumor** – the **intracranial pressures are elevated** but there's no tumor.
- Almost all patients are **women, obese**, and of **child bearing age**.
- There's a strong board association with **ocps** but other things can do it like vitamin A, isotretinoin, and glucocorticoid withdrawal.
- You'll see all the classic signs of intracranial hypertension (like **papilledema**).
- A **lumbar puncture** will reveal an opening pressure >25cm H_2O and the tap will relieve the headache.
- First line treatment is **acetazolamide.**
- Refractory disease is treated with **VP shunts** or serial LPs.

Trigeminal neuralgia

- Trigeminal neuralgia is essentially a seizure of the trigeminal nerve presenting with **lancinating pain** across or down the jaw and ear.
- They are often brought on by cold things in the mouth.
- It is a clinical diagnosis, though an **MRI** should be obtained to rule out compressive myelopathies.
- The treatment is **carbamazepine.**

Dz	Danger	History and Associated Sxs	Laterality	Quality	Duration	Aggravation	Dx	Treatment	PPx
Tension	Low	Vicelike headache, radiating to back and neck	Bilateral	Vicelike		Exercise	Clinical	Acetaminophen	N/A
Cluster	Low	Periorbital pain, rhinorrhea, lacrimation, Horner's	Unilateral	Boring	5-90 minutes many/day	∅	Clinical	100% O_2, Triptan	CCB
Migraine	Low	⊕ Triggers, photophobia, ⊕ N/V, ⊕ Aura, Disabling sxs, hangover	Unilateral	Pulsating	4-72 Hrs	∅	Clinical:	NSAID Mod: Triptan / Ergot	βB, CCB
Analgesic	Low	Pt uses pain meds >2-3 times per week	Any	Any		∅	Clinical	STOP Analgesic	N/A
SAH	High	Worst headache of their life, thunderclap headache	Bilateral	Tearing	Peaks in Seconds	∅	CT Scan	Surgery	N/A
Meningitis	High	Fever + headache Fever + Headache + Nuchal	Bilateral	Any	Acute	∅	CT	Surgery	N/A
Abscess	High	Fever + Headache + FND	Any	Any	Acute	Waking,	CT	Ceftriacone	N/A
Tumor	High	Worsening chronic HA, worse in AM, exacerbated by cough or Valsalva	Any	Any	Months	Waking, Cough	CT Scan	Rads/ Chemo	N/A
Idiopathic Intracranial HTN	Low	Abrupt onset N/V, s/s ↑ICP, Looks like a tumor, but isn't	Bilateral	Dull	Rapid Onset	Waking, Cough	LP	Acetazolamide Serial LPs, Shunts	N/A

SEIZURE

Introduction

- Seizures are **uncontrolled synchronous firing of neurons** in the brain.
- There are many different types of seizures with many different presentations.
- As such, they should be considered a **symptom** of an underlying disease.
- For the disease and appropriate intervention consider **epilepsy** (usually only with a history of this disease) and the **VITAMINS** mnemonic.
- Generally, go through the Section marked "Seizure/Vitamins" for a 1st time seizure, and then the section marked "Epilepsy" for repeat offenders.

Seizure/Vitamins

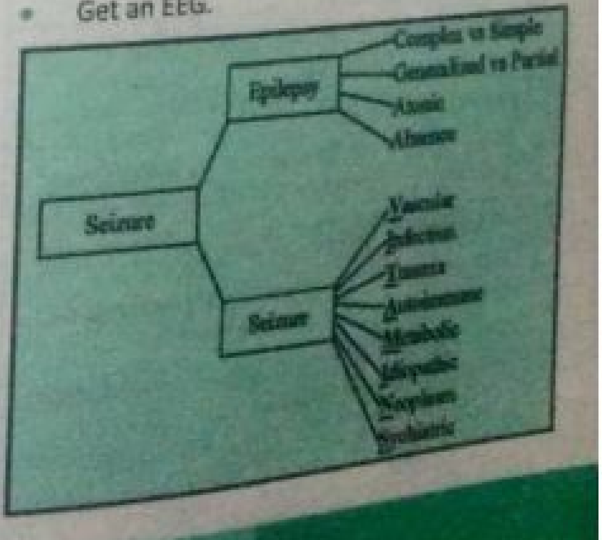
- On the boards, a new onset seizure will classically present as a grand mal.
- A grand mal seizure presents with **tonic clonic convulsions**, **bowel/bladder incontinence**, and **tongue biting**.
- Yet, all of these are very nonspecific.
- There's a **loss of consciousness**, but it's the **post-ictal confusion** that separates a seizure from alternative causes of loss of consciousness.
- A patient who has a seizure but is now normal requires observation, VITAMINS workup, and an EEG.
- However, when patients are actively seizing, are post-ictal, or have entered **Status Epilepticus**, they need to be **treated** as a **medical emergency**.
- The goal of treating a seizure acutely is to **reverse the underlying cause**.
- To do that the patient has to be alive - so the #1 priority is to **control ABCs** (intubation, oxygenation, ventilation, IVF).
- Before drawing labs to investigate VITAMINS the **seizure must be aborted**. Do so by following this cascade: (1) **IV/IM Benzos** (lorazepam / diazepam) → (2) **FosPhenytoin** →(3) **Midazolam** and **Propofol** → (4) **Phenobarbital**. Then **draw labs** and reverse any underlying defects.

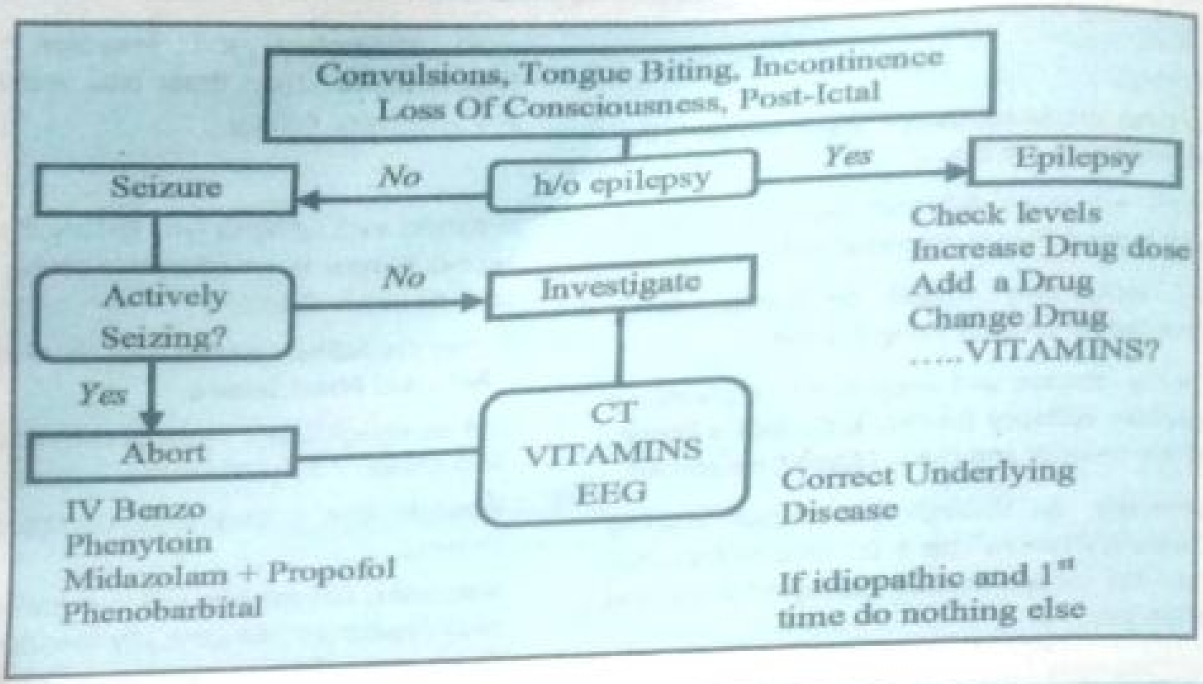
Epilepsy

- A patient with **epilepsy** (any history of seizure, repeat seizure in an idiopathic cause, etc) is treated a little different.
- If they are **actively seizing** treat them as above - **ABCs** and **Abort Seizure**.
- But an epileptic also requires chronic therapy to decrease the risk of another seizure.
- What to give is dependent on the type of seizure.
- **Valproate, lamotrigine**, and **levetiracetam** are broad spectrum and generally considered first line.
- As you dose patients it's important to reach **therapeutic levels** and **switch** if they **seize while therapeutic**.
- Diagnose the seizure and the location of origination with **EEG** by looking for **spike and waves** indicative of organized neuronal firing (abnormal for an awake adult). **24hr video monitoring + EEG** may be required to catch the seizure and its manifestations.
- For the test, you'll need to be able to identify certain types of seizure and link them with their treatment.

Non-convulsive Status

- The altered person, intubated, but no seizure activity.
- Get an EEG.




Convulsions, Tongue Biting, Incontinence
Loss Of Consciousness, Post-Ictal
h/o epilepsy
No
Yes
Epilepsy
Check levels
Increase Drug dose
Add a Drug
Change Drug
.....VITAMINS?
Seizure
Actively Seizing?
No
Investigate
Yes
Abort
CT
VITAMINS
EEG
IV Benzo
Phenytoin
Midazolam + Propofol
Phenobarbital
Correct Underlying Disease
If idiopathic and 1st time do nothing else

VITAMINS

Vascular	Stroke, AVM, Hemorrhage	FND + Risk Factors
Infxn	Encephalitis, Meningitis	Seizure + Fever
Trauma	MVA, TBI	h/o Trauma
Autoimmune	Lupus, Vasculitis, Arthritis	Rash, Purpura, ANA
Metabolic,	Na, Ca, Mg, O2	Glucose CMP, ABG, Mg, Phos
Idiopathic	"Everybody Gets One"	1st Time Seize
Neoplasm	Mets vs Primary	h/o Cancer, headache
Sychiatric	Faking it, Iatrogenic	Faking it / Hand Drop

Partial vs Generalized

Partial = Specific Complaint- **(Carbamazepine, Phenytoin)**

Generalized = Total Brain Involvement- **(Valproate or Lamotrigine)**

Complex Vs Simple

Complex = + LOC

Simple = - LOC

Specific Types

Atonic = + Loss of Tone, - LOC **Valproate**

Absence = - Loss of Tone, + LOC **Ethosuximide**

Myoclonic = Jerky Muscle **Valproate**

Trigeminal Neuralgia

STROKE

Intro

- Stroke is high impact; it's the **3rd leading Cause of Death** and a leader in lingering **morbidity**.
- Not only that, but it's a **preventable** and largely **time-sensitive** disease.

Etiologies

- Stroke is a **brain attack** - that is, an ischemic injury to the brain parenchyma.
- This can happen in three ways.

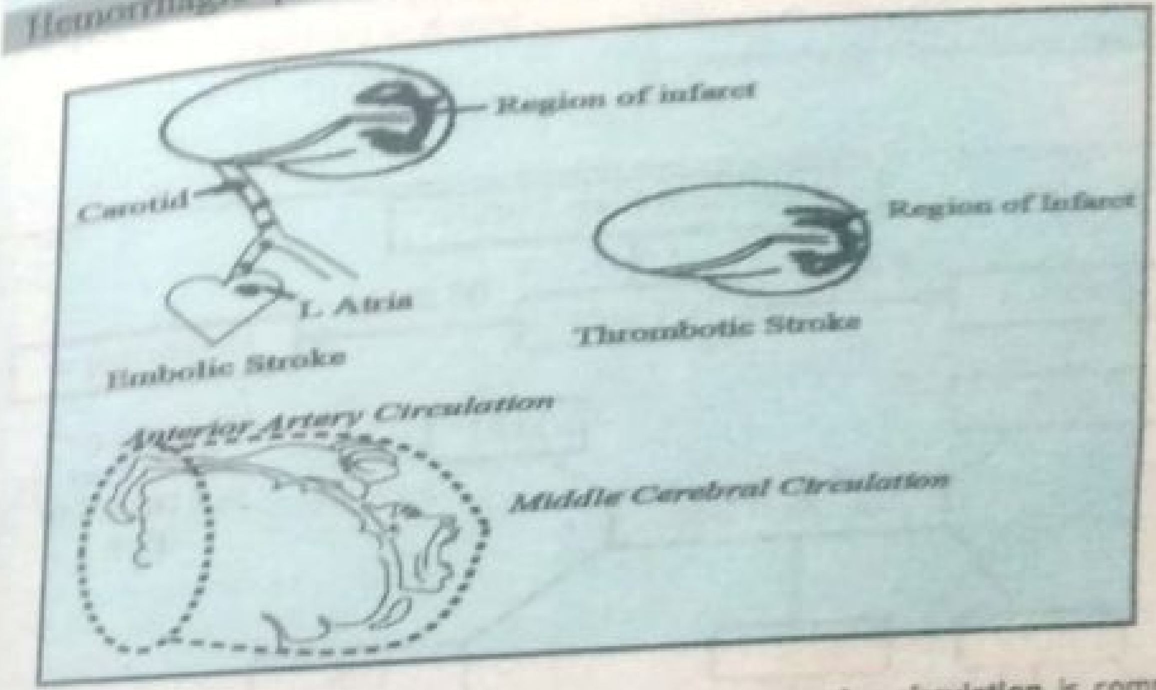
1) **Emboli** may form on diseased valves, in the left atrial appendage during Afib, or on a carotid dissection/stenosis. The emboli will then travel to a smaller vessel where it gets lodged in the lungs and occludes flow.

2) **Thrombi** may form in a vessel. This is the same pathogenesis as atherosclerotic plaque

in the heart, predisposed by CAD/PVD/HTN/ Atherosclerosis. Of the etiologies,

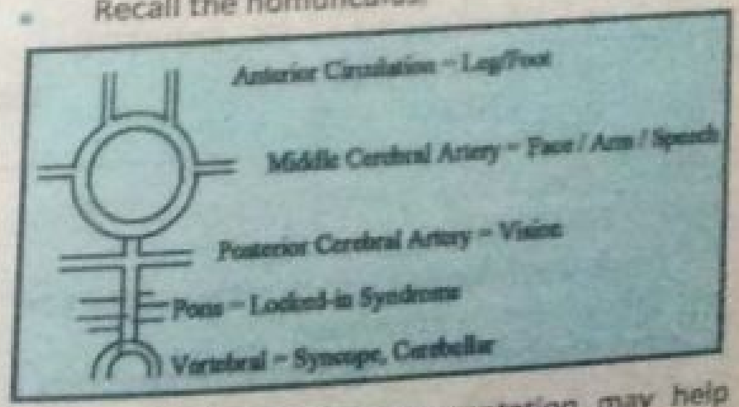
3) **Hemorrhage** has the worst prognosis. Both **subarachnoid** and **intraparenchymal hemorrhage** are considered "brain bleeds" - usually a product of hypertension. In this case blood does flow, just into the parenchyma. It's an irritant, decreases perfusion to the distal brain, and is a potential mass effect.

Etiology	*Type*	*Examples*
Ischemic	Embolus	Afib, Carotid Stenosis
	Thrombotic	CAD/PVD, Atherosclerosis, HTN
Hemorrhagic	Hemorrhagic	SAH, Intraparenchymal, HTN


Region of infarct
Carotid
L Atria
Embolic Stroke
Region of Infarct
Thrombotic Stroke
Anterior Artery Circulation
Middle Cerebral Circulation

Presentation

- The clinical presentation doesn't correlate with etiology.
- The tell-tale sign of any stroke is **Focal Neurologic Deficit of Acute Onset**.
- The location of infarct correlates to the defect.
- Thus a sudden onset loss of **motor, speech, sensation**, or **level of consciousness** prompts investigation.
- It becomes important to revisit arterial supply and vascular distribution.
- The **posterior circulation** is made of the **vertebral arteries** that come to form the **basilar artery**.
- Lesions here cause **cerebella dysfunction, Δ in Mental Status**, and **blindness**.
- The **anterior circulation** is comprised of the **anterior** and **middle cerebral arteries**.
- These feed the speech centers, motor strips, and sensory strips.
- Recall the homunculus.

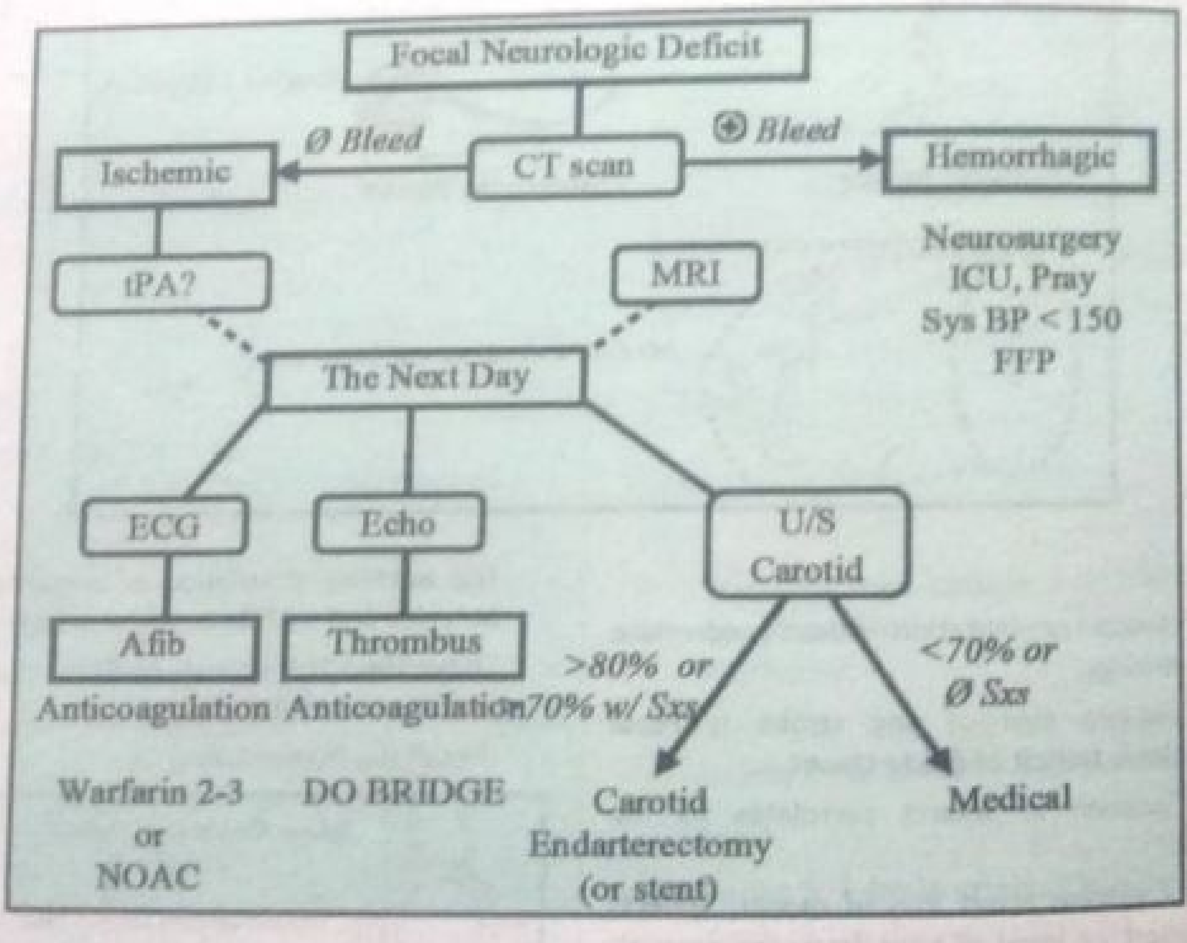

Anterior Circulation – Leg/Foot
Middle Cerebral Artery – Face / Arm / Speech
Posterior Cerebral Artery – Vision
Pons – Locked-in Syndrome
Vertebral – Syncope, Cerebellar

- Certain elements of presentation may help beyond simply location. For example, the patient with **Afib** has an increased likelihood of embolism.

- **Painful neck pulsations** and a patient who **grabs her neck** are indicative of a carotid dissection.
- **Patients** who've experience **TIAs** (FND < 24 hrs) in the past are highly likely to have a thrombotic event.

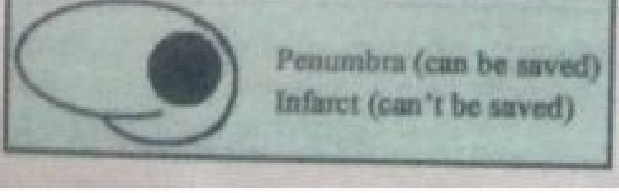
Diagnosis and Workup

- Regardless of presentation, in the **acute phase** of a stroke (**within 30 minutes** of presentation and **within 6 hrs of symptoms**) the goal is **rapid identification** and intervention if possible.
- The first thing to do is a **CT scan without contrast** to rule out hemorrhage.
- At this point therapeutic intervention is considered.
- After the initial presentation (usually on day 2), additional testing may be done.
- **Transesophageal Echo** assesses the cardiac valves, **carotid duplex** for carotid stenosis, **MRI** to look at areas of ischemia (CT scan is not to diagnose CVA, but to rule out hemorrhage), and **CT angiogram** for blood vessels of the brain.


Focal Neurologic Deficit
CT scan
Ø Bleed
⊕ Bleed
Ischemic
Hemorrhagic
Neurosurgery
ICU, Pray
Sys BP < 150
FFP
tPA?
MRI
The Next Day
ECG
Echo
U/S
Carotid
Afib
Thrombus
Anticoagulation
Anticoagulation
>80% or
70% w/ Sxs
<70% or
Ø Sxs
Warfarin 2-3
or
NOAC
DO BRIDGE
Carotid
Endarterectomy
(or stent)
Medical

Treatment Options

- Treatment is broken into the "treat right now" and "secondary prevention."


Penumbra (can be saved)
Infarct (can't be saved)

- If they present **within 4.5 hours** of symptom onset (**3 hours of diabetic**) they can be considered for tPA. It's the LAST TIME SEEN NORMAL. Which means someone who went to sleep normal and woke up with a stroke starts at the time they went to sleep. The big to-do for stroke is **tPA**, the **clot buster**.

- It has greatly restricted use but can actually rescue ischemic tissue and preserve the **penumbra**.
- The risk of transforming an ischemic stroke into a hemorrhagic one is high so caution must be used.
- Even if tPA isn't used the stroked brain will die. However, optimally controlling **oxygen >95%, tight glucose control 60-100**, and **Blood Pressure** (permissive hypertension) will allow the at-risk penumbra to recover.

tPA	ASA
Thrombotic / Embolic only Never if Brain Bleed Ever Sxs onset < 3 hrs Ø if surgery in 21 days Ø if head trauma	Primary med for secondary Prevention
Afib – Warfarin/NOAC	***Clopidogrel***
Embolic Stroke Prevention CHF HTN Age > 65 DM Stroke (worth 2)	Used when the patient can't tolerate ASA or when ASA fails. **probably going to be ASA + Clopidogrel in the future*

Test	Nots	*Timing*
CT scan NO contrast	Do it at presentation, rule out hemorrhage but is Ø useful to diagnosis CVA until days later	<30 min
ECG	Afib or not	Immediately
U/S Carotid	Carotid Visualization to rule out or rule in carotid artery stenosis and dissection	2nd Day
2D Echo	Visualize heart valves, especially in Afib, r/o source of embolism. TTE ↓Se, Easy TEE ↑Se, Difficult	2nd Day
CTA/MRA (not needed)	Visualize blood vessels, Ø require Angiogram	2nd Day
MRI	Visualize areas of ischemia, track resolution, confirm diagnosis if unsure	23 hrs

Treatment	*Notes*	*Chronic*
tPA	Ischemic stroke < 3 hrs + DM Ischemic stroke < 4.5 hrs + not DM Contraindicated with ICH, Bleeding, recent surgery or trauma	N/A
Heparin	Never	Never
Antiplatelet	1st Stroke: ASA Repeat Stroke: ASA + Dipyridamole ASA Allergy: Clopidogrel	Forever
Warfarin (NOAC)	Acute: Never Chronic: Afib with CHADS2 score 2+	Forever
BP	Ischemic no tPA <220/<120 Ischemic with tPA <180/<105 Hemorrhagic Stroke < 150 / 80	<140/<80 Ace-I
Biabetes	<140	A1c<7
Statin	High-Potency	High-potency

Most strokes occur and it's too late - nothing can be done for them - so preventing the next one becomes crucial.

Aspirin is the mainstay treatment unless the patient gets/has an allergy.

If there is an aspirin allergy, use **clopidogrel**.

If there's a stroke on aspirin, add a second agent - usually **aspirin + dipyridamole.** Newer literature is suggesting the use of aspirin + clopidogrel, but it hasn't hit the boards yet.

- For future stroke prevention, risk factor control is essential. This is what **medical management** means.
- Risk factor to medical management is as follows:

Dyslipidemia: High-potency statin

Diabetes: A1c < 7% (orals or insulin)

HTN: Ace-I and other agents

Smoking: cessation counseling

Antiplatelet: ASA first stroke, Add Second agent repeat on ASA (Dipyridamole vs Clopidogrel controversial)

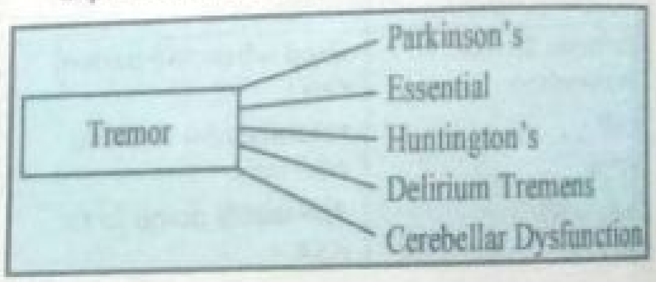
- In the condition where there's **carotid stenosis 80% or 70% and symptoms**, a carotid end-arterectomy may be performed. While a **carotid stenting** can be performed, it should be reserved only for those patients who CANNOT undergo surgery. Stenting and endarterectomy should **never** be performed in the acute setting; wait 2 weeks or more (going during a stroke worsens the stroke).

If there's **Afib** they need to be on **anticoagulation**. It doesn't matter whether you use **warfarin** (with an INR goal of 2-3) or the **novel oral anticoagulants** except that NOACs can't be used on valvular afib. **Neither needs a bridge**. Often, initiation of warfarin requires a heparin bridge. Afib is the one time where you definitely do **NOT NEED TO BRIDGE** (unless there is another indication such as a mechanical valve).

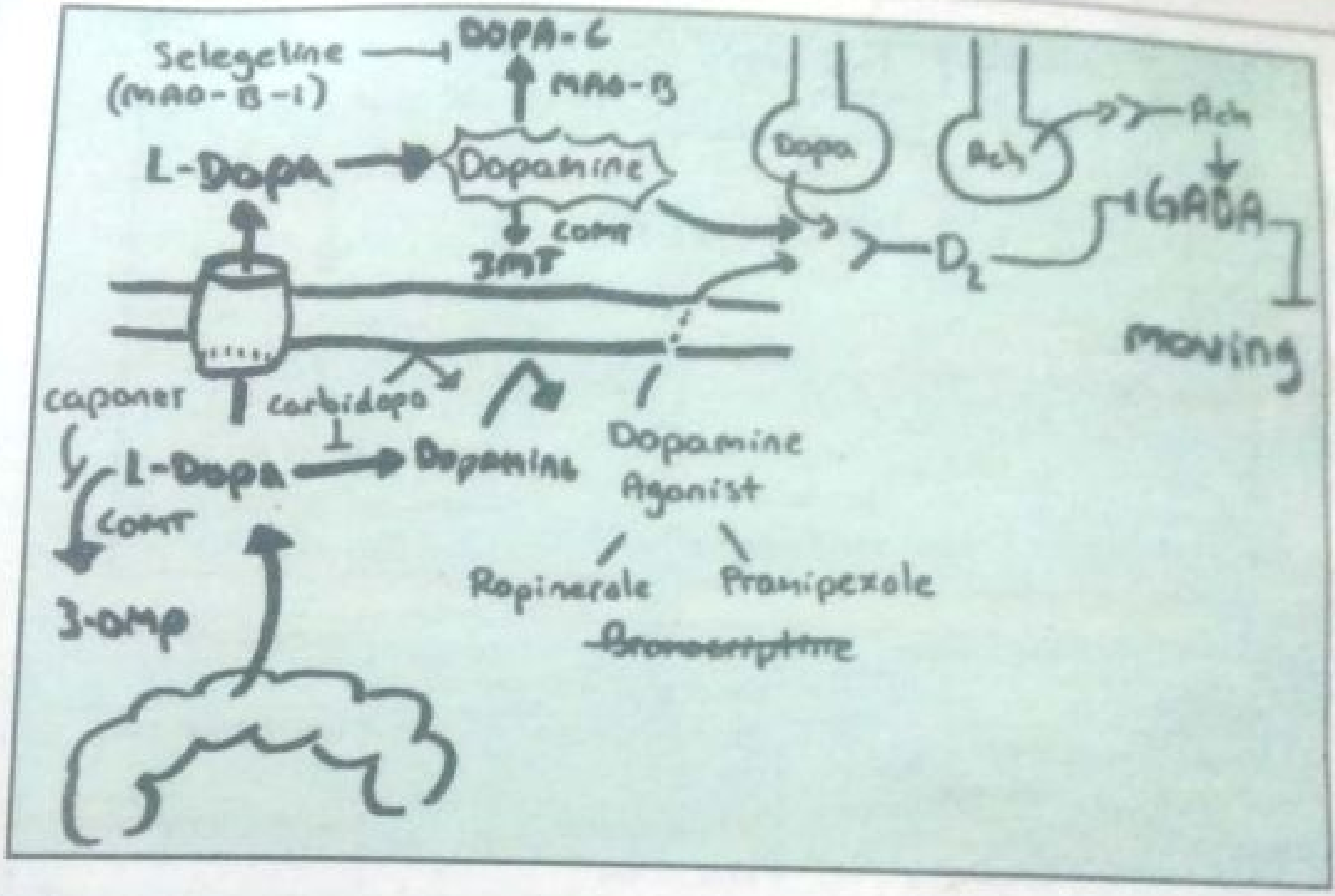
TREMOR

1) Parkinson's

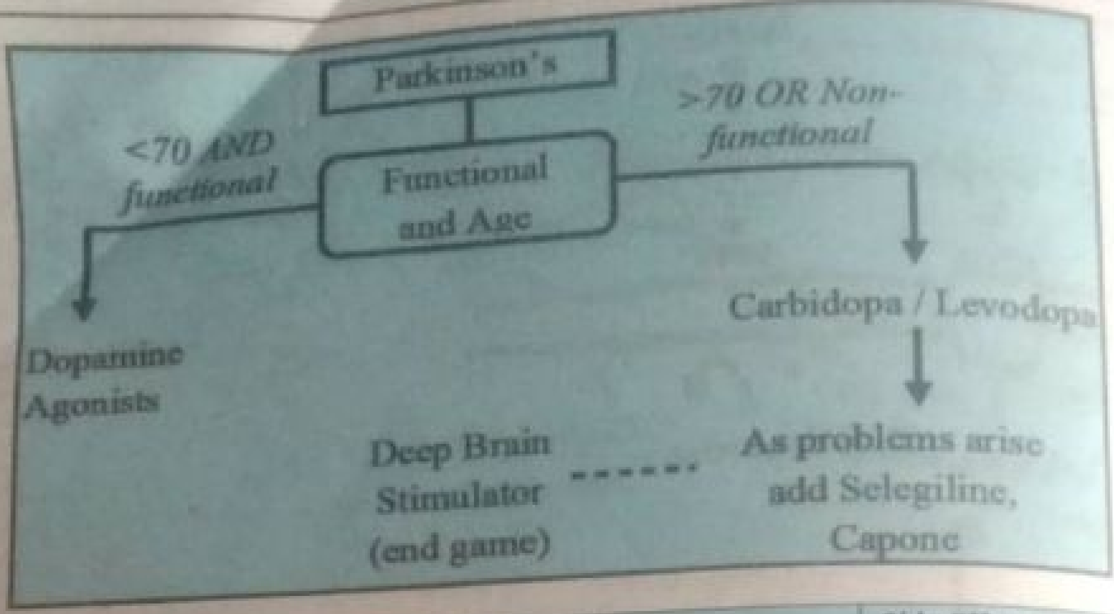
- Parkinson's is caused by a **Loss of Dopaminergic Neurons** within the **substantia nigra**. This essentially eliminates the "go" signal, preventing the **initiation of movement**. The ***classic symptoms of Parkinson's*** stems from **bradykinesia** (difficulty initiating movement). This will manifest itself in slow movements in general and even cognitive slowing.
- Logo for the classic **cog-wheel rigidity**, a resting **pill-rolling tremor**, and **gait disturbances / postural instability** (the little muscles that keep you straight up don't correct for position, so these patients are high risk for falls).
- The patient will have difficulty with the **get-up-and-go** test, and will walk with **shuffling steps**. A board buzz word is a **mask-like expressionless face**.



- The diagnosis is clinical.
- While brain imaging might be attempted to rule out something else (CT for a bleed, MRI for stroke), said imaging is not needed. The test might throw at you an **MRI of the substantia nigra** showing degeneration, but that is NOT needed for the diagnosis in life.
- Treatment is about the go signal. The go signal is dopamine. The stop signal is Acetylcholine. The focus of therapy is supplying the go signal.
- **Dopamine Agonists** agonists are the mainstay of therapy for **young, functional** people (<70, maintained function). Bromocriptine is an older, dirtier **dopamine agonist**, so the newer ones should be used instead. **Ropinirole = Pramipexole**.


Selegeline
(MAO-B-I)
DOPA-C
MAO-B
L-Dopa
Dopamine
COMT
3MT
Dopa
Ach
Ach
GABA
D_2
moving
caponet
carbidopa
L-Dopa
Dopamine
COMT
3-OMP
Dopamine
Agonist
Ropinerole
Pramipexole
~~Bromocriptine~~

- **Levodopa-Carbidopa** is the mainstay of therapy for everyone else (>70 or nonfunctioning). Levodopa CAN cross the blood brain barrier, carbidopa cannot. Carbidopa prevents the conversion of L-Dopa into dopamine. This means more levodopa gets into the brain, and more dopamine is created from more levodopa.
- But eventually, levodopa-carbidopa begins to **wear off**. The COMT-inhibitors and the MAO-B-inhibitors are brought in as levodopa-carbidopa begins to fail. There's no way to determine how to add them.
- Acetylcholine-R-antagonists like Benztropine could theoretically work, but the acetylcholine side effects are ***not worth it for the elderly***; the effect is also weak. Use this on young people who have a tremor only.
- While you DO want dopamine in the substantia nigra, the cost of "putting dopamine in the brain" is overstimulation of other dopamine tracts. In particular, it can **induce psychosis** with overstimulation of dopamine, causing schizophrenic symptoms and hallucinations. Remember, you use anti-dopamine drugs (antipsychotics) to treat schizophrenia. We haven't figured out how to target one tract over another just yet.


Parkinson's
<70 AND functional
Functional and Age
>70 OR Non-functional
Dopamine Agonists
Carbidopa / Levodopa
Deep Brain Stimulator (end game)
As problems arise add Selegiline, Capone

Drug	Mechansim	Indications	Side Effects
Amantadine		Functional >60 years old	
Carbidopa Levodopa	Dopamine Agonists	Nonfunctional	HoTN, Psychosis
Selegiline	MAO-B Antagonist	Nonfunctional Exacerbate	Delays Progression
Capones	COMT Antagonist	Nonfunctional Exacerbation	Delays Progression
Bromocriptine	Dopamine Agonist	Functional <60 years old	

HYPERKINETIC DISORDERS

1) Essential Tremor

- The essential tremor, also known as a **familial** tremor, is one that's **absent at rest but worsens with movement**.
- There's typically a family history of a tremor and it's often a man. It unfortunately doesn't have a treatment.
- Consider this when other causes have been ruled out already.
- For control of symptoms try **beta blockers**.

2) Intention Tremor = Cerebellar Dysfunction

- A tremor that's **absent at rest** and gets **worse the closer to the target** the finger gets.
- This is also called an intention tremor because it arises as the patient attempts (intends) to do something.
- Since there's a physical lesion (stroke, atrophy) of the cerebellum there's no therapy.

3) Huntington's

- Huntington's is an **autosomal dominant** genetic disease caused by **trinucleotide repeats.**
- The more repeats a person has, the earlier the disease sets in.
- Most people begin to exhibit symptoms near middle age (30-60).
- It also exhibits **anticipation:** occurring earlier and earlier in subsequent generations as the number of trinucleotide repeats expands.

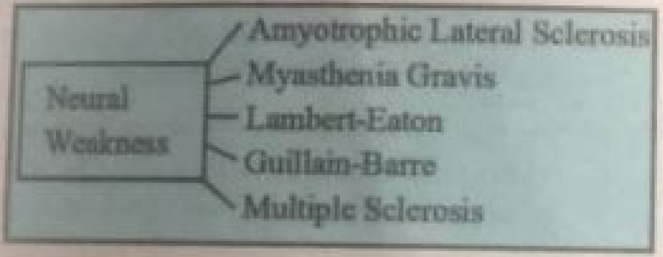
- Chorea is **purposeless ballistic movements**.
- The prognosis is terrible as it leads to dementia, psychosis, and often death by suicide.
- There's no treatment.

Disease	*Rest*	*Moving*	*Other*	*Tx*
Parkinson's	⊕	Improves	Old (>60)	Complex
Essential	⊖	Worsens	Middle (>30)	Propranolol
Cerebellar	⊖	Intention	Cerebellar Lesion	∅
Huntington's	⊕	Chore	Anticipation Trinucleotide rpt Suicide	∅

WEAKNESS

Introduction

- **Weakness** is a complicated complaint with a broad differential.
- Diseases can be broken down to demyelinating diseases, diseases of the neuromuscular junction, spinal cord lesions, lesions of the peripheral nerve, and lesions of the muscle itself.



- ALS – spinal cord
- Lambert-Eaton / Myasthenia = neuromuscular junction
- Multiple Sclerosis / Guillain-Barré = Demyelinating

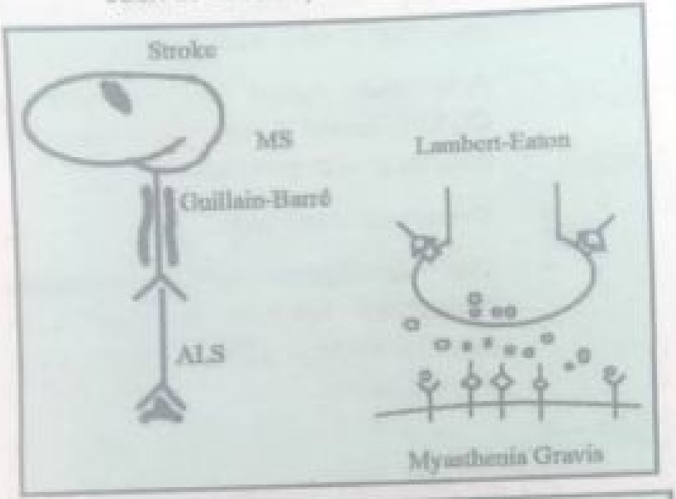
Amyotrophic Lateral Sclerosis

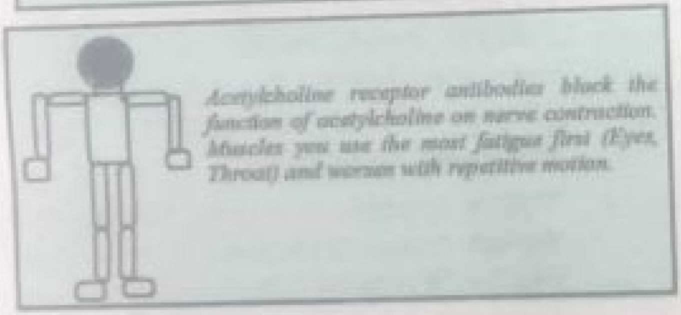
- ALS is a **chronic, progressive** disease of **unknown etiology** that produces **asymmetric Upper Motor Neuron** and **Lower Motor Neuron lesions**, generally sparing the eyes.
- Look for **atrophy** and **fasciculations** of the tongue and extremities commingled with **upward Babinski** and **hyper-reflexia** of the extremities.
- In late stage, LMN symptoms predominate.
- Associated symptoms are **emotional lability** and **weight loss**, though sphincter tone is maintained.
- Rule out spinal lesions with a CT/MRI/**Spinal X-ray** and confirm the diagnosis with an **EMG**.
- There's no treatment.
- The association with **superoxide dismutase** learned in step 1 is present in only 10% of cases; most are idiopathic.

Myasthenia Gravis

- An **autoimmune** disease targeting **post-synaptic Ach-R.** While the extremities may feel effect, the typical muscles affected are the **eyes** (Diplopia, Ptosis) and **throat** (swallowing).
- They're affected the most because the disease causes **fatigability** (Ach-blockade requires increased Ach concentrations to make the muscles work, depleting reserves).
- The fatigue is **relieved by rest**.
- On exam the patient will have **intact reflexes** and you may produce progressive weakness on repeated use.
- The initial test is the **Anti Ach-R Antibody** (nearly 100% specific with clinical symptoms).
- The best test is **EMG** showing decreased amplitude on repeated stimulation.
- **Pyridostigmine** is first-line therapy, thereby increasing **acetylcholine**

- If the disease is associated with a **thymoma** (diagnosed by **CT scan of the chest**), then a **thymectomy** may be curative.
- If the weakness compromises life functions (eating, breathing) then give either **IVIG** or **plasmapheresis** (you can't choose between them).
- Finally, refractory disease is treated with **prednisone** or disease-modifying agents such as azathioprine.

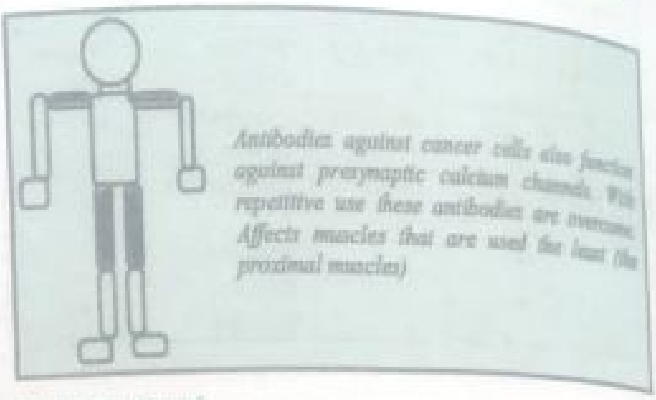




Acetylcholine receptor antibodies block the function of acetylcholine on nerve contraction. Muscles you use the most fatigue first (Eyes, Throat) and worsen with repetitive motion.

Lambert-Eaton

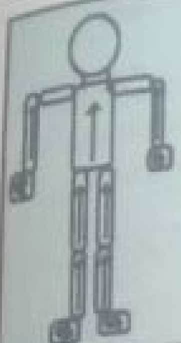
- Lambert-Eaton is a **paraneoplastic syndrome** producing an **antibodies** against **presynaptic Calcium channels**.
- This inhibits the release of Ach-vesicles.
- It produces a **proximal muscle weakness** that **improves with repeated use**.
- The clinical diagnosis is sufficient.
- However, the **antibodies** could be checked.
- A **CT scan** of the chest should be done to identify the small cell cancer causing the disease.
- The best test is an **EMG** showing improvement with repetitive use.
- The cancer is treated with **chemotherapy, radiation, or resection** (small cell lung cancer responds well to chemo and radiation).
- If cure is not possible, then symptom control is achieved with **prednisone** (palliative measures).



Antibodies against cancer cells also function against presynaptic calcium channels. With repetitive use these antibodies are overcome. Affects muscles that are used the least (the proximal muscles)

Guillain-Barré

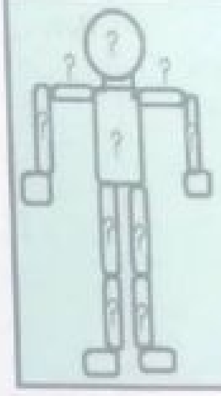
- Guillain-Barré is a demyelinating **autoimmune disease** that produces an **ascending paralysis** (weakness begins in legs, starting **distally, moving proximally**) 1-3 weeks after **diarrhea** (campylobacter) or **flu vaccinations**.
- There's always a **hyporeflexia** while **paresthesia** and **autonomic dysregulation** may or may not be associated. Because the ascension may reach the diaphragm (causing death) the first step is always to ascertain the need for **intubation**.
- To test for the disease look for evidence of autoimmune processes in the CSF with an **LP = lots of proteins, very few cells**.
- Confirmation is made with **EMG** and **Nerve Conduction Velocity** showing decreased nerve conduction velocity.
- Treat with **IVIG** or do **plasmapheresis** to **eliminate the causative** IgG Ab response **against myelin**.
- **While it looks and feels like autoimmune NEVER** give steroids.



Antibodies against myelin in the peripheral nerves begin most distally and work its way up. The demyelination is not permanent

Multiple Sclerosis

- MS is a disease with a presumed **autoimmune etiology** occurring in patients with a genetic susceptibility AND exposure to environmental triggers, creating antibodies against **myelin** (a **demyelinating disease**).
- It's difficult to diagnose MS based on only one presentation because it's defined by **neurologic symptoms separated by time and space** (blurry vision two years ago and now tingling in the arm for example).
- The ***primary complaint*** is often **blurry vision / diplopia** (from **optic neuritis**). If suspected, get an **MRI** looking for **periventricular plaques, multiple lesions,** or lesions on **corpus callosum**.
- ***Active lesions are easy*** to spot but older healed lesions may not be.
- Because it's often a **relapsing-remitting** disease (other forms are beyond the scope of a medical student) an MRI may be non-diagnostic. In this case, an **LP** with **pleocytosis** and **oligoclonal IgG** or **evoked potentials** may be done. These are ancient - like the Tensilon test - and aren't done. Because MS can linger there needs to be **chronic management** (**Interferon, Fingolimod, Glatiramer**), drugs for **acute flares** (**steroids**) and because it can cause any type of lesion in the cord, **symptomatic relief** for urinary retention (**Bethanechol**), incontinence (**Amitriptyline**), and spasticity (**Baclofen**).



Any nerve, motor, or sensory can be affected anywhere at any time then go back to normal just as suddenly.

	History	***Associated Sxs***	***Repeated***	***Diagnosis***	***Tx***	***Path***
ALS	Upper and Lower motor neuron sxs	Emotional Lability Weight Loss	N/A	XR Spine (normal) EMG	∅	?
Myasthenia	Chronic Fatigability of eyes and throat worse in PM or with use	Intact Reflexes Thymoma	Fatigue Worsens	1st Anti-Ach-R-Ab f/u with CT Chest Best EMG = Fatigue	Chronic: Prednisone Acute: IVIG Plasma Surg: Thymectomy Sx: Stigmines	Anti-AChR Post Synaptic

	History	*Associated Sxs*	*Repeated*	*Diagnosis*	*Tx*	*Path*
Lambert-Eaton	Proximal Muscle Weakness in a patient with Cancer	Cancer Symptoms (weight loss, hemoptysis)	Improves	CT Scan	Tx cancer, Prednisone Azathioprine	Anti-Calcium presynaptic antibodies
Guillain-Barré	Ascending Paralysis 1-3 weeks after diarrhea	Hyporeflexia, Paresthesia Autonomic Dysregulation	N/A	1st = LP = ↑Prot, ↓Cells Best = EMG	IVIG Plasmapheresis Ventilator	Autoimmune
Multiple Sclerosis	Neurologic symptoms separated in space and by time with a relapsing and remitting course in a female. Diplopia is most common	Any neurologic Symptoms	N/A	MRI (1st and best) LP (oligoclonal IgG) and Evoked Potentials only if MRI equivocal	Chronic: Interferon Acute: Steroids Incontinence: Amytript Retention: Bethanechol Spasticity: Baclofen Pain: Gabapentin	Autoimmune

POISONING

TOXIC INGESTION

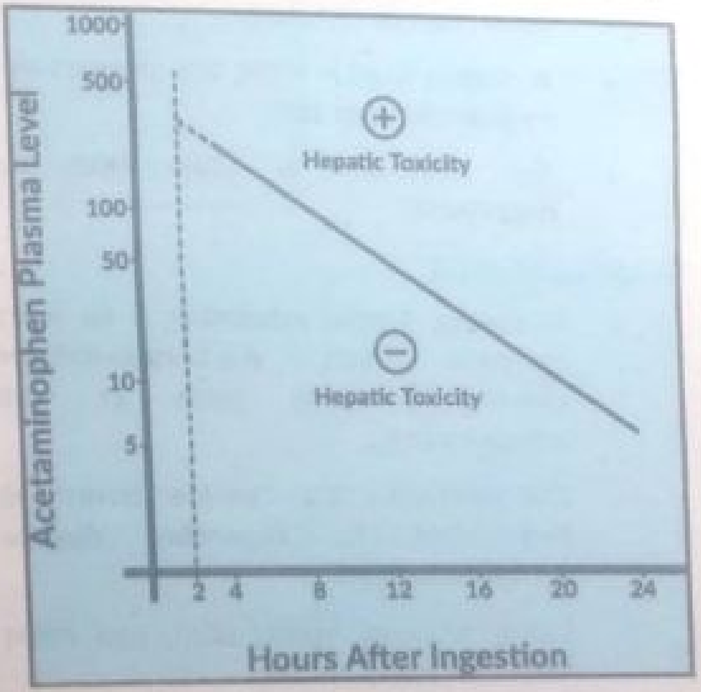
Alcohols

- Ethanol is covered in psychiatry.
- Look for cerebellar symptoms, nausea, vomiting, and amnesia.
- Support their airway, gives fluids, and then let them sleep it off.
- **Isopropyl** alcohol can be found in **rubbing alcohol**. It has similar effects to ethanol and can only be treated with supportive care. The difference is in the **osmolar gap** (elevated in Isopropyl, not in ethanol).
- **Methanol** (causes blindness, comes from moonshine) and **ethylene glycol** (kidney failure, comes from antifreeze) present and are treated similarly. Both yield an **anion gap acidosis** and an **osmolar gap**. Antifreeze has **fluorescein** in it to detect radiator leaks, so a **Wood's Lamp** can be used on the urine to make the diagnosis.
- The BMP will show whether there's an anion gap or not. **If no**, it's either Ethanol or Isopropyl - provide supportive care. **If yes**, it's methanol or ethylene glycol; inhibit conversion to the toxic metabolites by giving **Fomepizole** (if not available, alcohol will work).

Alcohol	*Source*	*Anion Gap*	*Osmolar Gap*	*Treatment*
Ethanol	Beverages	No	Yes	Supportive
Isopropyl alcohol	Rubbing Alcohol,	No	Yes	Supportive
Methanol	Moonshine	Yes	Yes	Ethanol Fomepizole
Ethylene Glycol	Antifreeze	Yes	Yes	Ethanol Fomepizole

Acetaminophen

- Acetaminophen overdose causes **drug-induced liver injury**. Whether it's by intentional ingestion (a bottle of pills) or unintentional overdose (narcotics taken together with acetaminophen), the result is the same.
- Look for **elevation of liver enzymes** (this can be into the thousands).
- Obtain an **acetaminophen level** at 4 and 16 hours.
- If they're above-the-line on the nomograms (don't worry about memorizing the numbers), give the antidote called **N-Acetylcysteine** (NAC) IV. If they develop fulminant hepatic failure, transplant may be needed.



[illegible]ity

- Aspirin and other salicylate products (Oil of Wintergreen, or "headache powders") can cause intoxication.
- Early in the disease there's **tinnitus,** vertigo and **hyperventilation** (look for the respiratory alkalosis).
- Late in the disease **anion-gap metabolic acidosis** predominates; the patient becomes altered, obtunded, and **hyperpyrexia** predominate.
- Obtain a salicylate level, and treat with **alkalization of the urine** and forced diuresis.

Carbon Monoxide Poisoning

- Because carbon monoxide has a **much higher affinity** than oxygen for hemoglobin, inhalation of carbon monoxide produces **carboxyhemoglobin,** a hemoglobin that can't carry oxygen.
- And yet, the **saturation of hemoglobin is NORMAL** when read by pulse oximetry.
- Carbon Monoxide comes from inhaled smoke.
- Headache, nausea and vomiting, and **delirium** are symptoms.
- When suspected, a **carboxyhemoglobin level** must be obtained.
- A normal level is < 3%, but smokers may have as much as 10%.
- The treatment is **100% FiO2** and **hyperbaric.**

Cyanide Poisoning

- In reality, **Smoke inhalation** is far more common than medication-induced cyanide poisoning (such as with nitroprusside).
- The person is sick as Cyanide converts all metabolism to **anaerobic despite adequate oxygen.**
- Coma, seizures, hypotension, and heart block are late symptoms.
- Look for **cherry-red skin color** and **cherry red arterial blood.**
- The first line therapy is **thiosulfate** - the second line treatment (amyl nitrate) may worsen Carbon Monoxide poisoning.

Organophosphate Toxicity

- Whether used as **weapons of terror** (VX nerve gas), **medications** (Oglivie's syndrome, myasthenia), or as **pesticides** exposure to organophosphates can be fatal.
- **Initial exposure** reduces the effectiveness of Acetylcholine esterase. Eventually it renders it to permanently irreversibly inactivated ("aging").
- Everything that can secrete something will.
- Treatment is with **atropine** and **pralidoxime** ("2-pam chloride").

S	Salivation
L	Lacrimation
U	Urination
D	Defecation
G	Gastrointestinal upset
E	Emesis

PHARMACOLOGY—TOXICITIES AND SIDE EFFECTS

Specific toxicity treatments

TOXIN	TREATMENT
Acetaminophen	*N*-acetylcysteine (replenishes glutathione)
AChE inhibitors, organophosphates	Atropine > pralidoxime
Antimuscarinic, anticholinergic agents	Physostigmine, control hyperthermia
Arsenic	Dimercaprol, succimer

Benzodiazepines	Flumazenil
β-blockers	Atropine, glucagon
Carbon monoxide	100% O2, hyperbaric O2
Copper	Penicillamine, trientine (Copper penny)
Cyanide	Nitrite + thiosulfate, hydroxocobalamin
Digitalis (digoxin)	Anti-dig Fab fragments
Heparin	Protamine sulfate
Iron	Deferoxamine, deferasirox, deferiprone
Lead	EDTA, dimercaprol, succimer, penicillamine
Mercury	Dimercaprol, succimer
Methanol, ethylene glycol (antifreeze)	Fomepizole > ethanol, dialysis
Methemoglobin	Methylene blue, vitamin C (reducing agent)
OpiOids	NalOxOne
Salicylates	NaHCO3 (alkalinize urine), dialysis
TCAs	NaHCO3 (stabilizes cardiac cell membrane)
Warfarin	Vitamin K (delayed effect), fresh frozen plasma(immediate)

PSYCHIATRY

DRUGS OF ABUSE

Alcohol Intoxication

- **Alcohol** is among the **most common** abused substance in the United States (and the world).
- It lends itself to the identification of addiction to other substances. It also follows the lecture on substance abuse disorder. Some facts: affects **males > females** (3:1), clusters in **families**, highest prevalence is in **Native Americans and Alaskan Natives**, patients have high **risk for suicide, accidents, violence, and TBI**.

EtOH DEPENDENCE

S/S Withdrawal	**HTN and Tachycardia**
PPx Withdrawal	**Benzo** (also treatment)
Wernicke's	**Reversible** Cerebellum
Korsakoff's	**Irreversible** confabulation

- Acute alcohol intoxication includes **disinhibition, amnesia** (blackouts), cerebellar dysfunction (**ataxia**), and as the toxic level rises, **nausea, vomiting,** and death.
- Alcohol is unique in that it's **zero-order** metabolism – no matter how much you give the liver, it can only process **0.03/hr** which allows an reverse extrapolation during criminal investigation.
- The legal limit of intoxication for driving a car is 0.08.
- The rate of processing EtOH does not change – its 0.03 /hr (one standard drink). But the tolerance does.
- A chronic alcoholic can tolerate a 0.3 level.
- A non-chronic drinker would be severely toxic at 0.20. One drink (12 oz beer, 5 oz wine, 1.5 oz liquor) is about 0.03.
- Further, alcohol compromises the ability to metabolize sugar through a **thiamine deficiency,** which is why we give the "coma cocktail" **thiamine** then D_{50}.
- Long-term alcohol use can lead to the **reversible cerebellar dysfunction (Wernicke's)** and to the **irreversible confabulation** and **cerebral atrophy (Korsakoff's)**.
- Alcohol use predisposes to cirrhosis, **GI bleeding, Varices, Mallory-Weiss** and a host of other diseases.
- Maintenance treatment for alcohol use disorder consists of long term **group therapy** (AA) and medication.
- **Antabuse** (causes a disulfiram-like reaction), **Naltrexone** (also indicated for opioiduse disorders), or **Acamprosate** can be used to facilitate treatment compliance.

Acute EtOH Intoxication
Blood Alcohol Concentration > 0.08 (2-3 drinks)
Breathalyzer screen
Detox Rate is 0.03/hr = reverse extrapolation during criminal investigation
"Found Down" = **Thiamine** and then **D50**

EtOH Screen CAGE
Cut down?
Annoyed by criticism?
Guilty about drinking?
Eye opener to get started?

Alcohol Withdrawal

- Alcohol withdrawal is **life-threatening.** Benzo withdrawal is identical to Alcohol withdrawal.
- Other than BZD and EtOH, **no other withdrawal is fatal.**
- EtOH and BZD stimulate GABA, which is inhibitory.
- Constant stimulation of an inhibitory signal causes the GABA to be downregulated.
- If the depressant (EtOH, BZD) is acutely withdrawn, the inhibitory signal is reduced and excitation occurs.
- **Excitation** is the name of the game in identifying EthH withdrawal, as well as assessing response to therapy.
- The CIWA score is a subjective "objective" tool; when it's used by the same provider it has utility in tracking symptoms and response to therapy.

EtOH Withdrawal

+/- N,V	HTN + tachycardia
+/- Headache	Tremors
	Diaphoresis
	Confusion
	Seizures

- Alcohol (and benzo) withdrawal typically happens **48-72 hours after the last drink.**
- The first things seen are **diastolic hypertension** and **tachycardia** as the autonomic nervous system gets excited.
- They'll pass through **tremors, diaphoresis,** and **anxiety** ("bugging out"). When they become **confused,** they're on the doorstep of **seizures (delirium tremens).**
- Intervene before that happens.
- Treatment of alcohol (and BZD) withdrawal starts with a **long acting benzo** (chlordiazepoxide or diazepam) with **rapid acting benzos as needed.**
- Taper the long-acting to off, and give IV or PO benzos to keep the patient near baseline.

EtOH Withdrawal Treatment

Long-Acting BZD	Short-Acting BZD
Chlordiazepoxide	Lorazepam (IV)
Diazepam	Alprazolam (PO)
Taper These	PRN these

Opioids

- **Prescription opioid** use has become a leading cause of **overdose deaths.**
- Many patients ultimately addicted to **heroin** start out with prescription narcotics from physicians or dentists.
- Opioid withdrawal **isn't life-threatening,** but is extremely uncomfortable with muscle aches, sweats, chills, stomach cramps, vomiting, diarrhea, irritability, runny nose, goose bumps, and sneezing.
- **If a patient in opioid withdrawal experiences seizures, suspect withdrawal from benzos or alcohol or underlying seizure disorder.**
- **Withdrawal** treatment is largely symptomatic in both outpatient or hospital settings, depending on severity and use. Replacement is with other opioid-containing medications, like **Methadone or Suboxone; Clonidine** can also be used.
- **MAT** (Medication Assisted Treatment) for maintenance treatment also consists of **Methadone, Suboxone,** or **opioidantagonist Naltrexone.** Preferred treatment during **pregnancy** is **Methadone.**
- **MAT** has been shown to reduce opioid relapse rates.

Drug	*Intoxication*	*Withdrawal*	*Drug / Antidote*
EtOH	Slurred speech, Disinhibition, Ataxia, Blackouts, Memory Loss, Impaired Judgment	Tremor, **Tachycardia**, HTN, **Seizures**, Psychosis	Benzo Taper (withdrawal)
Benzos	Delirium in elderly, **Respiratory Depression** and **coma** (with ↑ dose), amnesia	Tremor, **Tachycardia**, HTN, **Seizures**, Psychosis	Flumazenil
Optiates	Euphoria, **pupil constriction, respiratory depression**, and potential **tract marks**	**Yawning**, lacrimation, N/V and hurts everywhere, sweating	**Naloxone** **Methadone** (long-term)
Cocaine	Psychomotor agitation, **HTN, tachycardia, dilated pupils, psychosis** **Angina / HTN** crisis	Depression, suicidality, "cocaine Bugs	Supportive Care or Benzos α then β blockade
MDMA	**Overheat** (fever, tachycardia) and **water intoxication**. Pupillary Dilation, Psychosis	Crash	Supportive
PCP	**Aggressive** psychosis, **vertical horizontal nystagmus**, impossible strength, blunted senses	Severe random Violence	Haloperidol to subdue **Acidify Urine** to enhance excretion
LSD	Rarely seen, Hallucinations, Flashbacks, heightened senses	Flashbacks	Supportive
Marijuana	Tired, slowed reflexes, **conjunctivitis**, the **munchies**, overdose brings **paranoia**	Ø	Supportive (often nothing required)
Barbiturates	Low safety margins, Benzos safer	Redistribute into fat	Ø
Nicotine	None - just jittery and stimulated. Pt has to OD to go into a Vfib	Cravings	**Bupropion** **Chantix (Varenicline)**
Amphetamines	Tachycardia, hypertension, pressured speech, flight of ideas	Crash	Ø

SUBSTANCE ABUSE DISORDER

Introduction

- This deals with two separate, but very related issues.
- One is **substance abuse disorder**; it requires a bunch of boxes to be checked on a checklist AND impairment socially, financially, or with work/school. It's the **impairment** that makes it a disorder.

- The other issue is **addiction**, which is more than substance abuse disorder. It'll be explained further in the coming pages.
- While we're focusing on **substance abuse**, the same principals can be used on any vice – gambling, sex, or any substance.

Substance Abuse Disorder

- Substance abuse disorder consists of usage despite cognitive, behavioral, and medical complications of use.
- In life it's **really hard** to tell when someone has a disorder versus socially acceptable norms.
- It'll be easy on the test – they'll have florid disorder that's usually severe (lots of checks on the checklist).
- There are **four major categories** to help you remember the checklist. ^{1}Controlling use, ^{2}social impairment, ^{3}risk-taking, and ^{4}physical/pharm changes.

Difficulty Controlling Use

1.	Consuming more than was intended
2.	Difficulty cutting down or stopping use
3.	Invests time in obtaining or recovering from use
4.	Craving
Adverse Social Circumstances	
5.	Failed responsibilities at work, school, or home
6.	Use despite social/relationship problems
7.	Giving up important school, job, and other activities
Risk-Taking	
8.	Use in hazardous situations (legal issues: sex, driving
9.	Use despite previous consequences or complications
Health Effects	
10.	Tolerance: requiring more for the same effect
11.	Withdrawal: physical symptoms when stopped

- The **severity** is based on **how** many checks the patient gets. There are a total of 11. It ranges from **Mild** (2-3), to **moderate** (4-5) and **severe** (6+). Because patients with substance abuse either **don't know they have it** or are judged (aka they know **to hide it from you**) it's important to keep an eye out.
- There are two screening tools to help a busy practice pick up on people who might be missed: **CAGE** for adults, and **CRAFFT** for adolescents. If they have **any one** a more in depth investigation (running this checklist) is a good idea.

• GAGE=Adults	CRAFFT=Adolescence
Cut down, trying to quit the substance Anger or Annoyed by criticism about using Guilty about use or things you do while using Eye opener to get started in the day	Car-using it while driving Relax – using the substance to wind down or relax Alone – using the substance of its own Friends – LOSING friends Forget – memory loss because of use Trouble – with family, law, Teachers

Made for EtOH, applicable to basically any substance.

- The problem is that some patients **may not want to talk about it** or might be in flat denial.
- Excluding very specific drugs like EtOH and tobacco, **pharma doesn't work**. There **is no one answer** for everyone, though group therapy (alcoholics anonymous) and psychotherapy are the mainstay of treatment.

Five Stages of Substance Abuse

Pre-contemplative	Unaware, denial
Contemplative	Admits there's a problem, acceptance
Preparation	Committed, taking steps
Action	Actual changing behavior
Maintenance	Sustained changed behavior

- **Most people will relapse.** Relapse isn't failure - it's just a relapse. Get people back on the wagon and off the drugs.
- Patients often temporarily have remission and **high relapse rates**, or return to substance use after a period of abstinence, **50-90%** of the time. Because addicted patients often present as a result of a crisis, it's important to know brief intervention strategies to promote change.
- The goal here is to identify the **5 stages of quitting** and being able to **FRAME** the way you talk to your patients.
- Experimental substance use often begins during **adolescence**, with use of highly-accessible substances such as alcohol, nicotine, inhalants, and cannabis; they're often referred to as '**gateway drugs**' since users frequently advance to addiction of benzodiazepines, opioids, cocaine, etc.

Motivational Interviewing

F	Offer Feedback
R	Emphasize personal **Responsibility** – taking ownership for sobriety and their success
A	Give **Advice** – its ok to chime in
M	**Menu** of option – no one thing works for everyone, so try a bunch of things
E	Use **Empathy** – addicts will trick you, but everyone else treats them like garbage. You shouldn't
S	Support **Self-Efficacy** and show them how life is better while clean

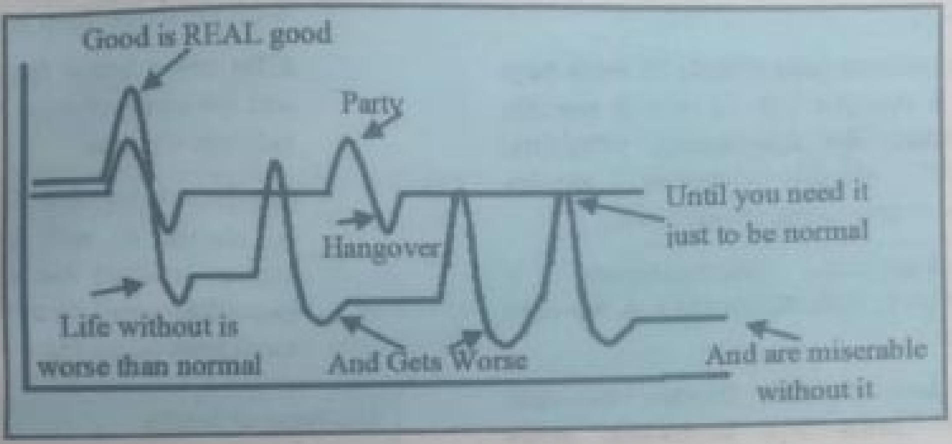
Addiction

- Addiction is more than substance abuse – it's a **neurobiological disease** where the person who uses does so **to feel normal.**
- Addicts have a **genetic predisposition to addiction**, but there are also social and environmental determinants leading to a maladaptive pattern of use.
- Most children will **experiment** – they do it at parties, with peer groups and friends. Most people who try drugs and alcohol **don't become addicts**.
- However, the **earlier drugs** are tried **the more likely the user is to become an addict**. This is correlation - not causation - but the correlation is compelling (and likely reflects the genetic predisposition).

To understand the problem with addiction, let's compare two competing timelines.
The non-addict goes through life. They're average normal. They have ups and downs. But then they go out on Friday night. They get dinner and a half bottle of wine. They feel good. They Uber home. The next day, they're back to normal. But THEEEEEEN... they take Step 1. And phew! Done! They get HAMMERED. Fun that night. But the next day... ugh... hung over. After a bowl of Pho, a box of Pedialyte, and a liter of lactated ringers they recover. And... back to normal (the normal happiness associated with the brutality of medical training).

- The addict goes through life. They're average sub-normal. They have ups and downs. Then they try a substance. Their first high is better than anything the non-addict will ever experience. The problem is that after the high wears off the addict is way worse, on average, then before they used. So they use again, trying to get that same high. But eventually, they **use to feel normal.**

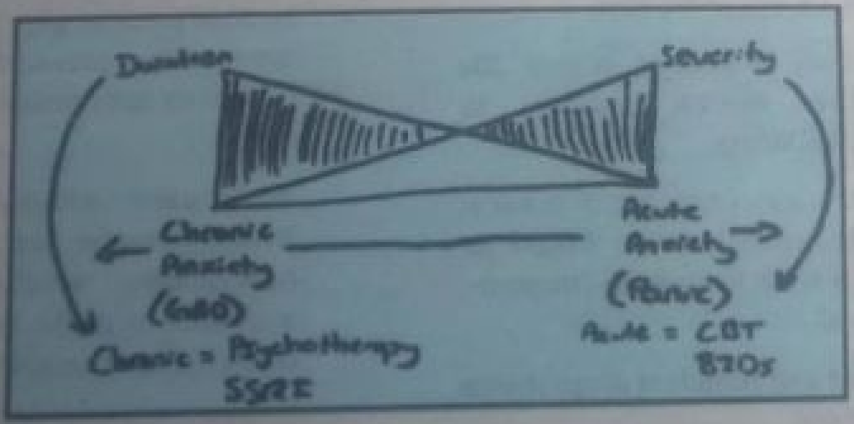
- Addicts will cheat, lie, and steal. They will dupe you. You will be tricked. Their families are fed up. The health care system is judging them. They **will relapse**. But if you **use empathy**, don't judge them, and see that there's a neurobiologic mechanism - an actual disease - you will change someone's life.


Good is REAL good
Party
Until you need it just to be normal
Hangover
Life without is worse than normal
And Gets Worse
And are miserable without it

ANXIETY DISORDERS

Introduction and Comorbid conditions

- **Anxiety** is a diffuse response without a precise feeling involving **worry, fear,** and **hyper-vigilance**, coupled with its physical symptoms: **palpations, perspiration**, and **dyspnea.** Everyone has felt the sinking feeling in the pit of their stomach before opening a letter about their big test grade or a phone call from the parents at 2 AM bearing bad news. This is what anxiety's all about. Some anxiety is provoked by **triggers** (places and things), but it can also be in a **constant state**.
- In adulthood, patients with anxiety disorders often concurrently develop depression, while some cope with anxiety by drinking alcohol excessively. Anxiety disorders are more common in **women.** Children often experience separation anxiety, phobias, and social phobias. Adults often outgrow them, but some persist.
- See anxiety on a spectrum of **chronic, insidious** anxiety that is usually low in severity, but almost always present (GAD) and **acute, severe** anxiety that can strike at any time (Panic). The subsequent anxiety-related disorders will fall somewhere in between. The concept is that when anxiety is severe (and strikes quickly), the goal is to **abort the attacks** (benzos, CBT). But Benzos should not be chronic therapy, whereas most diseases have a **chronic component** which will usually respond to **chronic control** with **SSRIs** or **psychotherapy**. This may not be intuitive yet, but it will be after impulse, OCD, and PTSD lessons.


Duration
Severity
Chronic Anxiety (GAD)
Acute Anxiety (Panic)
Chronic = Psychotherapy SSRI
Acute = CBT BZOs

1) Generalized Anxiety Disorder – CHRONIC

- Patients who have **constant anxiety** about **almost everything** in life will spend a lot of time worrying and worrying about worrying.
- These patients have anxiety on **most days** of **> 6 months** and have **> 3 somatic symptoms** like restlessness, irritability, fatigue, muscle tension, trouble concentrating, sleep changes, etc.
- If diagnosed, **psychotherapy** is paramount. PSYCHOTHERAPY is the right answer.
- Long term medical therapy for GAD include **SSRIs** and **buspirone**. While benzodiazepines can be used to treat panic disorders, and GAD can have panic disorders, the use of benzodiazepines to treat GAD is definitely the wrong answer. BZD for Panic attack only.

Constant state of worry about

Most things on Most days

- *≥ 6 months / years*
- *≥ 3 somatic complaints*
    - *Irritability*
    - *somatic pain*
    - *weight change*
    - *sleep change*
    - *concentration*

2) Panic Disorders – ACUTE

- Patients will experience **Panic Attacks** ("STUDENTS PANIC") that come **without provocation,** i.e. out of the blue.
- Onset is usually in **females** in their **20s** without other medical problems to suggest medical illness.
- Panic Attacks can resemble a medical disease (MI, Asthma); those should be ruled out if it's the first attack (troponin, ecg, peak flow).
- **Hyperthyroid** and **stimulant drugs** should also be ruled out.
- Once a panic disorder is diagnosed three things can be done.
    1. **Abort the attack** with **benzos.** But because of their addictive potential, don't prescribe them long-term.
    2. **SSRIs** are a better long term choice and are more effective than cognitive behavior therapy.
    3. Cognitive Behavioral Therapy should be started as well, often used to control or abort the attacks without benzodiazepines rather than prevent them from occurring.

Shortness of Breath
Trembling
Unsteadiness
Depersonalization
Excessive heart rate
Numbness
Tingling
Sweating
Palpitations
Abdominal distress
Nausea
Intense fear of losing control/dying
Chest pain

2b) With or without Agoraphobia

- Because patients get random attacks that come without provocation, there may also be fear or anticipation of having them in public.
- Both panic attacks and generalized anxiety disorder can be modified with **Agoraphobia**, which is the fear and avoidance of public areas, crowds, public transportation, or going outside alone.

3) Phobias

- Specific phobias are **irrational** and **exaggerated fear** of an **object** or **situation**. They produce **anxiety** and **avoidance** of the stimulus.
- They're generally considered to be learned responses.
- They're **common in childhood** along with separation anxiety and selective mutism, but most are outgrown in adulthood.
- Those that persist are generally considered pathologic and, if they cause the patient lost productivity or are overtly ego dystonic, require treatment.
- Those that **commonly persist in adulthood** are **social phobia** (public speaking, urinating in shared bathrooms, being in crowds) and **specific phobia** (clowns, spiders, heights, flying).

) Social Phobias

- The situation is often one where **potential embarrassment** could occur (public urination, public speaking).
- The test will almost always test you on **beta-blockers** (atenolol, nadolol, or propranolol) being used for **public speaking** (also called performance anxiety or stage fright).
- Really, cognitive behavioral therapy... sometimes just practice... is what the patient needs.

3b) Specific Phobias

- It's common to hear of people afraid of heights, spiders, or flying.
- The fear comes from somewhere.
- Because it's learned we try to learn serenity in the place of anxiety.
- This in one of two ways: systemic desensitization (slower, more effective over time, longer duration of success), or flooding (faster, less effective over time, but can get adequate control quickly).
- **Systemic Desensitization** involves stages of anxiety-provoking situations, each of which are **conquered sequentially** using medications or techniques to control anxiety during the session. Starting over with a small amount of anxiety-provoking stimulus (being in an elevator) and controlling the anxiety reaction is how to begin. Eventually, the patient will have an increasing severity of stimulus after the previous level is conquered (the 12th floor of the hotel after the 11th). This breaks the stressor-to-anxiety relationship, and gradually the severity of the stressor can be increased until no medications are required to control the anxiety, even when confronted with the stressor. This is the **best treatment** and should be done for people looking for a long term solution to their phobias.
- **Flooding** is performed by overwhelming the patient with a major stimulus while engaging in anxiety-reducing behaviors or under medication. Rather than gradually step them up, they are exposed to so much stimulus that the anxiety response "burns out." Choose flooding when there is a **time-sensitive need** (an actor must go into a cave for a shoot) but long-term anxiety reduction isn't required (that actor may never go to a cave again).

CATATONIA

- Catatonia isn't a diagnosis; it's a physical state that's used to **modify the diagnosis** of a mood or psychiatric condition.
- While it can be associated with medical conditions (autoimmune, paraneoplastic, steroids), Catatonia should be associated with **bipolar, depression,** and (less frequently) schizophrenia). Back in the day the term "catatonic" was used to categorize a motionless variant of schizophrenia, but is now known to be more associated with **mood disorders** than psychotic disorders.

A big change in DSM-V is that catatonia is no longer tightly associated with schizophrenia (it used to be a sub-category of schizophrenia); it's now strongly associated association with mood disorders (bipolar, depression schizoaffective) instead.

Catatonia is defined by at least 3 of the following:
Stupor - ↓ alertness and ↓ response to stimuli **Catalepsy**- pt can be put in any position **Waxy flexibility** – slight, even no resistance to positioning (and holding) **Mutism** - no verbal response when once there was **Negativism** – motiveless resistance to instructions **Stereotypy** – repetitive, non-goal directed movements **Agitation** or **Grimacing** **Echolalia** – mimicking speech **Echopraxia** – mimicking movements.

- Fixing the underlying condition is paramount to treatment.
- When encountered, **lorazepam** is the treatment of choice.
- Lorazepam can be both **diagnostic and therapeutic**.
- Refractory cases are treated with **ECT**.
- But because they DON'T move… or eat… and they can do this for hours to days, they'll need help with **nutrition** and are at increased risk for **DVT** and rhabdomyolysis (↑ CK).

Forms of Catatonia

Retarded Catatonia	Mutism, Posturing, Negativism, Staring
Excited Catatonia	Hyperkinesis, frenzy, combativeness, Restless
Malignant Catatonia	Rigidity, Autonomic instability (↑ HTN, ↑ HR, ↑ Temp)

Cataplexy is for narcolepsy

Cataplesy is for Catatonia

Psych+Catatonia versus Psych+Drug-Induced Cataoniaoid

- I made up the word "Catatonia-oid."
- Catatonia can lead to immobility, fever, and an elevated CK level from muscle breakdown. This is a modifier of the psychiatric disorder. But some psychiatric diseases are treated with medications. Some medications can induce conditions that are, for all intents and purposes, indistinguishable from malignant catatonia. These diseases look like catatonia and are often associated with an elevated creatine kinase, rigidity, and fever. Differentiating malignant catatonia (**non-drug** induced) from NMS (**antipsychotic** induced), Serotonin syndrome (**SSRI** induced), and malignant hyperthermia (**anesthesia** induced) is based (at your level) only on the medications that caused it.

Differentiating Diseases

Malignant Catatonia	Rigidity, Autonomic Instability, ↑ Temp, pysch, but no drugs
Neuroleptic Malignant Syndrome	Rigidity, Autonomic Instability, ↑ Temp, ↑ creatinine kinase, anti-psychotic medications
Serotonin Syndrome	Rigidity, Autonomic Instability, ↑ Temp, ↑ creatinine kinase, SSRI-s
Malignant Hyperthermia	Rigidity, Autonomic Instability, ↑ Temp, ↑ creatinine kinase, Halothane anesthesia

- **Neuroleptic Malignant Syndrome** also presents with delirium, autonomic instability, fever, and elevated creatinine kinase. NMS is seen with **atypical antipsychotic** medications.

- *Olanzapine, Risperidone, Ziprasidone Quetiapine*

- **Serotonin Syndrome** also presents with delirium, autonomic instability, fever, and elevated creatinine kinase. The **lead-pipe rigidity** (myoclonus and hyper-reflexia) and use of **SSRIs** helps differentiate Serotonin syndrome form the others.

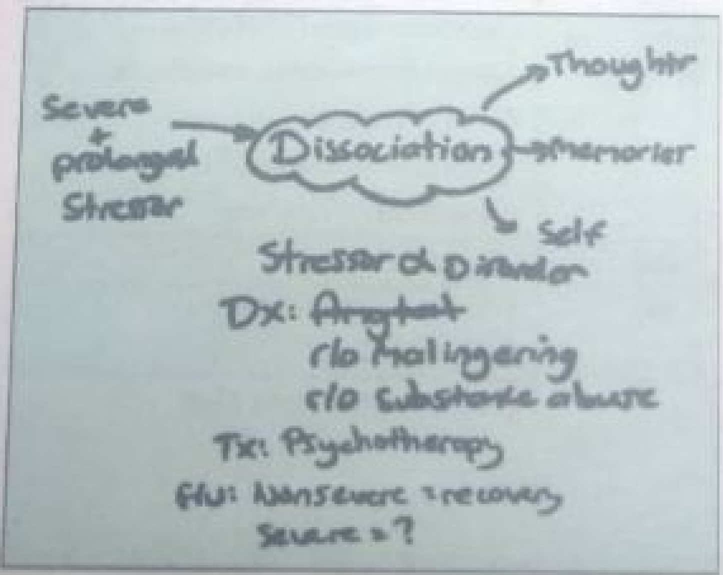
- *Venlafaxine, Duloxetine, Paroxetine, Fluoxetine, Sertraline, Citalopram, Escitalopram*

- **Malignant hyperthermia** also has autonomic instability (aka fever), rigidity, ↑ creatinine kinase, but it occurs with administration of an anesthetic gas such as **halothane**. There's often no psychiatric diagnosis or psych meds, though there may be a family history. Use **Dantrolene** to reverse the effect.

DISSOCIATIVE DISORDERS

Introduction

- Essentially, dissociation means things are **happening** ***around*** us but we feel as though they're **not happening** ***to*** us.
- We're **consciously unaware** despite our **unconscious participation**.
- This can be reconciled by "zoning out" - thinking about something else while driving.
- We get to the intended destination but fail to remember the drive. Some dissociation is normal; too much is pathological.
- Usually, the psychologic stressor is **tremendous** and **prolonged**.
- The more severe the stressor, the more severe the response.
- We discuss each disorder in order of descending severity.
- For each, the goal is to **identify the disorder**, ensure it's **not malingering or substance abuse**, then use **psychotherapy** to repair.
- This is a fairly rare set of disorders, and their vocabulary might seem circular.
- We attempt to separate them clearly into distinct disorders for test prep purposes.


Severe + prolonged Stressor
Dissociation
Thoughts
Memories
Self
Stressor of Disorder
Dx: ~~Amytal~~
r/o malingering
r/o substance abuse
Tx: Psychotherapy
f/u: Nonsevere = recovery
Severe = ?

1) Dissociative Identity Disorder

- This is effectively **multiple personalities**, requiring **two or more** distinct identity states.
- There's a question whether identities abruptly take over the person or if there's an overlapping transition (it's likely either can be true).
- The patient experiences **recurrent gaps in memory** ("blackouts") or suffers from **inconsistencies** in everyday events or important personal information.
- People who know the patient, or interact with them regularly will notice changes in **affect** and **behavior,** often completely out of character and manifesting as **paradoxical behaviors** (doing things they would otherwise never do).
- This commonly arises from periods of **intense** and **prolonged stress**.
- The primary personality develops the others to protect the self (the others are hurt while the primary is shielded).
- This requires **intense psychotherapy** and **hypnosis** to correct, often aligning the personalities into one.

Dissociative Identity Discorder

Path:	≥2 distinct identity states Most severe and prolonged trauma
Pt:	Self-experiences - Memory Gaps (blackouts) - Other dissociation symptoms Others Witness - Paradoxical behaviors - Appearance changes
Dx:	Clinical
Tx:	Intense Psychotherapy and Hypnosis

Movies: Sybil, Fight Club

Dissociative Amnesia

Path:	Stressors induces loss of memory
Pt:	Memory Loss of - the event - regular everyday occurrences / routine - complete autobiographical self

2) Dissociative Amnesia

- Defined as the **inability to recall** or **inconsistency in recall** or ordinary important information.
- It's often associated with an **acute emotional trauma** or **stressor**.
- The loss of memory is usually focused on the **event itself**, but can also include everyday routines or memories, or even loss of the entire autobiographical self.
- More severe forms may find a patient adapting to a new identity, while mild forms may simply have the inability to recall the stressor.
- If there's travel, it's deemed **dissociative fugue**, a subtype of Dissociative Amnesia.

Law and Order: SVu Dissociative Amnesia with Fugue

Path:	Stressors induces loss of memory WITH Travel
Pt:	Memory Loss of - the event - regular everyday occurrences / routine - complete autobiographical self

Movies: Long Kiss Goodnight, Jason Bourne

Shows: Archer (FX) becomes Bob (Fox)

3) Dissociative Amnesia with Fugue

- Dissociative Amnesia **with purposeful travel** or **bewildered wandering**.
- If there's travel, it's fugue.

4) Depersonalization Derealization Disorder

- **Depersonalization** is the experience of detachment from own thoughts, body, or actions – as if you're watching a movie about yourself.

- **De-realization** is the experience of detachment from surrounding, as if living in a dream. It's typically seen in **adolescents** with a **benign stressor** (which may be relatively severe).

Depersonalization Derealizatoin Disorder

Path:	Adolescent with benign (relatively major) Stressor
Pt:	Seeing a video or dream of self, out-of-body experience (depersonalization) Detached from reality, as though in a dream Reality testing INTACT

EATING DISORDERS

thods used in eating disorders

- **Restriction** is the act where weight loss is achieved through dieting, fasting, and extreme exercise. No calories ever go in; it's predominant in anorexia nervosa.
- **Binge-purge** is the act where there's copious eating (the binge) and then some form of elimination (the purge). If **emesis** is the method of evacuation, there will be a **metabolic alkalosis** and **Elyte abnormalities**. Signs of emesis include **parotid** swelling, dental erosion and dorsal hand scars.
- **If laxative** use is the method, look for **metabolic acidosis** and (not surprisingly) diarrhea.

Restriction	↓ Caloric intake (fasting, dieting) ↑ Caloric expenditure (exercise)
Binge Purge Emesis	Eating / Binging then induced emesis Dorsal hand scars (from emesis) Dental erosion (from emesis) Metabolic Alkalosis, K, Mg disorders
Binge Purge Laxative	Eating / Binging then induced diarrhea Metabolic Acidosis Diarrhea

The appearance of the patient is often dependent on the disorder, not the method she uses.

Anorexia Nervosa

- Anorexia Nervosa is a severe body dysmorphic disorder.
- The patient (10:1 F:M) **fears getting fat** or **believes she is fat** despite being underweight, AND there's a **lack of recognition** of how seriously underweight she is.
- The classic patient is a **woman** who is **underweight** and **malnourished**: **amenorrhea**, emaciation, lanugo, cold intolerance.
- Severe signs include **bradycardia, leukopenia,** and **hypotension**.
- If a girl is **<85% ideal body weight** or **extreme anorexia** (BMI < 15), she should be hospitalized. This requires force feeds, intravenous nutrition, and often electrolyte replacement.
- **Cognitive behavioral therapy** is critical to control the dysmorphic aspect. Medications are usually directed at comorbid conditions – SSRI/SRNI for Major depression or OCD (**fluoxetine**), and anti-psychotics can be used as primary treatment.
- Most will relapse in 5 years. Deaths result from **suicide** and **medical complications.**

Anorexia Nervosa

Anxiety	Is thin, fears getting fat, thinks she's fat
Method	Restriction (can purge)
Weight	Underweight
Tx:	CBT + Antipsychotics SSRI/SnRI if OCD or MDD
F/u:	Hospitalize if ↓BMI or E-lytes Relapse common in 5 years Death from medical or suicide

WHO Severity by BMI

Severity	*BMI*
Mild	> 17
Moderate	16-16.9
Severe	15-15.9
Extreme	< 15

Anorexia nervosa is categorized by the WEIGHT

Bulimia Nervosa

- Bulimia Nervosa patients also fear getting fat and have an unrealistic self-body image. However, the anxiety is more a product of the **action (Binge)** than the weight **body image.** Bulimics often have a normal or **overweight BMI**. The behavior associated with Bulimia is binge: eating abnormally large amounts of food / a lack of control during eating. But after, the patient may have inappropriate compensatory **behaviors**: **purge**, fasting, or excessive exercise. These compensatory behaviors happen at least once a week for 3 months. Treatment centers around fluoxetine and CBT.
- **Never give bupropion** in Bulimia as there's an increased risk of seizures. Weight loss medications are also contraindicated in Bulimia.

Bulimia Nervosa

Anxiety	Binge, feeling ashamed
Method	Purge (can restrict)
Weight	Normal weight (or overweight)
Tx:	SSRI (Fluoxetine), CBT
F/u:	Bupropion causes seizures

Bulimia Severity

Severity	***Compensatory behavior / week***
Mild	1-3
Moderate	4-7
Severe	8-13
Extreme	> 14

Bulimia nervosa is categorized by the PURGE

Binge-Eating Disorder

- It's Bulimia, except there's **no purge** and the patients are **overweight**.

Other Eating Disorders

- **PICA** is the eating of non-food substances for **over a month**. These non-food substances must not be expected given developmental age. Look for soap, paint, paper, air, or chalk. This will most likely present as a toxicity from the ingested substance.
- **Rumination Disorder** involves regurgitation of food for a least a month. It's mostly in infants, or those with developmental problems. It's related to overfeeding and the inability to cope with the sensation of fullness.
- **Avoidant / Restrictive Food Intake Disorder** is characterized by a lack of interest in eating food; it's accompanied by weight loss, nutritional deficiency, or the need for supplementation. It also happens in infancy and early childhood.

GENDER DYSPHORIA

Gender Terminology

- **Gender Assignment** happens at birth; the child is either male or female. Legally speaking this is determined by the **external genitalia**. Specifically, the genotype is erroneous - only the external genitalia determines the assignment.
- **Gender Identity** is what is in the person's brain. It's what they believe they are. This can be defined as male, female, or other.
- **Transgender** is a broadly used term to describe patients temporarily or persistently identifying with a gender different from what they've been assigned.
- **Transsexual** is a patient who physically or socially transitioned from one sex to another. Not required to be transsexual, but when present essentially confirms the diagnosis is physical transition via surgery or hormones to become more like the opposite gender.
- **Transvestic disorder:** ("Transvestite") is a condition of **crossdressing behavior** resulting in sexual excitement, causes distress, but is usually NOT associated with gender dysphoria.
- What's up with gender vs sex? Gender is identity, while sex is biology. In life they're used interchangeably.

Gender Terms

Assignment	Your genitals at birth "What you are physically"
Gender Identity	Your gender in your mind "What you are mentally
Transgender	Someone who's identity is more often incongruent than their assignment
Transsexual	Not only identifying, but has socially or physically changed to another assignment
Transvestic Disorder	Cross-Dressing but NOT transgendered

Gender Dysphoria

- Gender dysphoria is a combination of **incongruent identity** (by definition, transgendered) that also **causes distress**.
- It can be characterized by the feeling that they are the opposite sex, the desire to change themselves to be the opposite sex, or even wanting to rid themselves of all sex characteristics ("asexual" in idiom).
- It can be defined as easily as believing they have the typical feelings of another gender.
- In children, all that may happen are instances of **cross-dressing, assuming stereotyped roles** of the opposite gender, or **rejecting stereotyped roles** of the same gender.
- Children may also just be having fun; cross dressing isn't necessarily an intentional decision, so be careful.
- To be sure it isn't more than just dress-up, there must be

  1) some sort of distress and 2) a duration of activity > **6 months.**

Gender *Dysphoria*

Duration > 6 months AND any one:
1. Incongruence between experienced gender (gender identity) and sex characteristics (assignment)
2. Desire to be, be treated as, or have sex characteristics of another gender
3. Wanting to rid self of sex characteristics
4. Beliefs that the patient, the self, has typical feelings and reactions of another gender *a.* Be cautious with stereotyping here

> *Be cautious of the idiomatic use of the words and their clinical definition. Also* ***very low yield*** *for the test.*

Paraphilia

- Defined as a condition in which a person's sexual arousal and gratification depend on fantasizing about or engaging in sexual behavior that's atypical or extreme.
- It's unfortunate for the people who have them; what's totally normal to the "patient" is viewed as unacceptable by society. To separate "kinky" from "disorder" consider a paraphilia to be distinguished as a preoccupation with the object or behavior to the point of being dependent on it for sexual gratification. Often, the person is gratified sexually by the specific act, which requires intense therapy or incarceration if it violates another's rights.

Defining Paraphilias

COMMON

Pedophilia	Sexual focus on children. Often Male adult à female child
Exhibitionism	Exposing genitals to strangers
Voyeurism	Observing private activities of unaware victims
Frotteurism	Touching, rubbing or a non-consenting person

UNCOMMON

Fetishism	Inanimate objects
Masochism	Being humiliated or forced to suffer
Sadism	Inflicting humiliation or pain on others
Transvestic disorder	Sexually aroused by cross dressing

Homosexuality

- Is **NOT** considered a disease or disorder.

IMPULSE CONTROL

Introduction

- Impulse Control disorders are a subset of Anxiety disorders.
- **Impulses** are **anxiety-inducing** needs to do something.
- **Actions relieve anxiety** (or cause pleasure).
- You can see the similarity between Obsessions and Compulsions in OCD disorders.
- These diseases are linked together because the actions can be **associated with crimes** (opportunity to separate out from malingering).
- It's the **stressor, action,** and response to the action that separates these diseases.
- Medications, therapy, and combination therapy all work equally poorly, and consideration for **incarceration** needs to be had.

DSM-IV linked impulse control disorders with depleted serotonin, and thought SSRIs would be helpful. DSM-V has removed that association – usually nothing works to reduce the incidence of actions.

Intermittent Explosive Disorder

- There's a **stressor** (usually physical, violent, or loud) that induces anxiety.
- The **action** is some **violent act** that's **out of proportion** to the initial stressor.
- That violent act is directed at people or property.
- After the act the patient is **calm, relaxed,** and without remorse.
- The **diagnosis** is dependent on frequency and **severity**: either **twice** a **week in 3 months** WITHOUT harm or **three times (at all) in a year** WITH harm.
- It's more commonly seen in **men**.
- The **symptoms** tend to lessen with age.

MOOD DISORDERS

- Mood I integrates two elements of DSM-V: Depression and Bipolar.
- They're combined because the predominant features (aka what you need to know) have cross over / similarities.
- We focus on major depression (depression), bipolar I (mania), bipolar II (hypomania), and the longer duration variants dysthymia (depression) and cyclothymia (bipolar).

DEPRESSIVE

Major Depressive Disorder

- To qualify for major depression there must be at **least 5** of SIGECAPS, which must include **depressed mood** or **anhedonia** for at least **2 weeks.**
- Depression appears more frequently in women (2:1). There are two major types of MDE: **melancholic** ("typical") and **atypical.**
- With **melancholic depression,** patients slow down. They **sleep less, eat less,** and **lose weight;** the "typical" features.
- With **atypical depression**, however, there are cases where people **sleep more, eat more,** and **gain weight;** "atypical" symptoms.
- All **SSRI/SNRI** medications are ***first line***, are indistinguishable from one another, and are equally efficacious.
- Combination therapy with **SSRIs** and **psychotherapy** is better than either alone.
- When starting an SSRI, an adequate trial of **4-8 weeks at maximal dosing** is required before adding a second agent.
- If a patient is failing medications and therapy, or if there is catatonia or psychotic features, the ultimate best treatment is **electroconvulsive therapy** (ECT).

	Typical	*Atypical*	
SLEEP	↓	↑	Insomnia / Hypersomnia
Interest	↓	↓	Anthedonia
Gulit	↑	↑	Inappropriate Guilt
Energy	↓	↓	Fatigue
Concentration	↓	↓	
APPETITE WEIGHT	↓	↑	Weight Gain/Loss
Psychomotor	↓	↓	Slow Thoughts, movement, speech
Suicidal	↑	↑	If suicidal, it is an MDE

Anti-depressants have ↑ risk of suicidality
- Motivation before mood

Depression with Suicidal Ideation

- What's most important is to look for **suicidal tendency,** then hospitalize if present.
- Assessing the intention, ability, and validity of the threat are all paramount.
- Removing a patient's rights and imprisoning them for their safety requires certainty.
- If there are suicidal ideations AND a plan, hospitalize.
- If there are suicidal ideations but no plan, safety contract.
- If there are no suicidal ideations, use SSRI, SNRI.

Dysthymia – Persistent Depressive Disorder

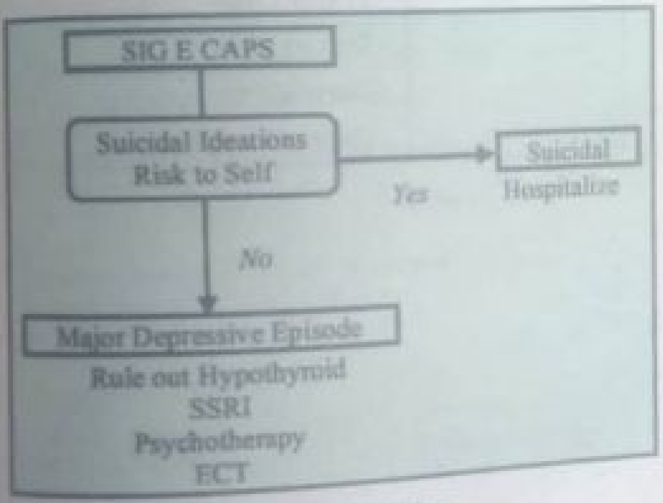
- This is essentially chronic depression, but not severe enough to be considered MDD.
- The patient will experience a **depressed mood** for **> 2 years** but without symptoms >2 months at a time.

Scanned with CamScanner

- This patient will be **functioning** but will have **depressed mood**.
- This is the person you get the feeling is depressed, but doesn't meet the severe symptoms of an MDE.
- We treat them the same - rule out **hypothyroid**, rule out suicide, and give **SSRIs**.

Disruptive Mood Dysregulation Disorder

- Kids having constant irritability with recurring behavioral outbursts, disproportionate to situations. Happens at least **3x per week**, and is evident **before 10 years old** (manifests ages 6-18).



Premenstrual Dysphoric Disorder

- Women must have at least 5 symptoms in the week before onset of menses, start to improve within a few days of onset, and they must be absent in the week post-menses.
- Look for accompanying mood swings, irritability, depressed mood, anxiety, lacking interest, difficulty concentrating, changes with appetite and sleep, breast tenderness, muscle pain, bloating.

BIPOLAR

Bipolar I

- Bipolar type I is ***mania-predominant***.
- Manic symptoms can be remembered by the mnemonic DIG FASTER (to the right).
- To be classified as Bipolar I, the patient must have "E" with **another 3 symptoms** for at **least one week**.
- Bipolar disorder has equal rates in men and women.
- Suicide is 15x higher in bipolar patients.
- Bipolar can be characterized as mania, but may also have modifiers for catatonia, rapid cycling, peripartum, and psychotic features.
- If a patient requires hospitalization, has psychosis, or has had a true manic episode, the patient must be diagnosed as Bipolar I, not Bipolar II.

DIGFASTER Mnemonic for Mania

Distractibility	Distracted
Insomnia	↓ Need for Sleep
Grandiosity	Self-Importance
Flight of Ideas	Cannot Follow Conversations
Agitation, Activities	Multiple Incomplete Projects
Sexual Exploits	Spending Sprees, Promiscuity
Talkative	Pressured Speech
Elevated mood	
Racing thoughts	

↓

1) ER: **Benzo**

(2) Life-Long = **Lithium or Valproate**

(3) Comorbid = **Carbamazepine** or **Lamotrigine**

Bipolar II

- Bipolar II is **hypomania** AND **major depression**.
- There must be a current or previous major depressive episode to be diagnosed bipolar.
- Hypomania is defined by all the same symptoms of mania, except they are **less**

severe (not as impairing), and for **less time** (at least 4 days).

Cyclothymia

- Bipolar I is mania. Bipolar II is hypomania with depression.
- Cyclothymia is Bipolar II, just not as bad.
- Patients have had **at least 2 years** of hypomanic and a major depressive episode, plus symptoms that fails to meet the criteria for Bipolar II.

Treating Bipolar Disorders

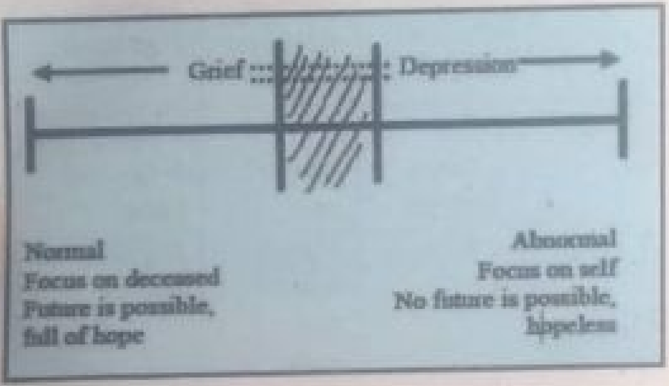
- In general, the goal is to **avoid anti-depressants**.
- A manic episode can be provoked (revealing the underlying bipolar disorder) by use of them.
- Even if major depressive episode is predominating, if it's known they're bipolar avoid SSRIs.
- **Mood stabilizers** are the mainstay of therapy. **Lithium** is the classic mood stabilizer. It has a narrow therapeutic index, can rapidly become toxic in renal failure, and has a dirty side effect profile including diabetes insipidus, vomiting / abdo pain, and progresses to encephalopathy, ataxia, and hyperreflexia. Other mood stabilizers such as **valproate**, **carbamazepine**, and **lamotrigine** can be used.
- **Anti-psychotics** such as quetiapine can be used in all phases of treatment, but are generally going to be the wrong choice on the test. Quetiapine is a safe bet in all cases. **Benzos** can be used to subdue a manic patient in the ED.

Depressed	Quetiapine Lurasidone Olanzapine -Fluoxetine
Manic	Mood Stabilizers - Lithium - Valproate - Carbamazepine Antipsychotic - Olanzapine - Aripiprazole - Risperidone - Ziprasidone - Chlorpromazine
Maintenance	**Mood Stabilizers** - Lithium - Lamotrigine **Antipsychotics** - Olanzapine - Aripiprazole - Risperidone - Ziprasidone - Chlorpromazine

MOOD– LIFE AND DEATH

Introduction

- DSM-IV had Grief / Bereavement and Depression.
- DSM-V has added persistent complicated bereavement disorder.
- This makes things harder. See these as two concretely different diseases - grief and depression - and PCBD being "in between."
- **Grief** has a shorter duration, with a mild depressed mood, but all the attention and sadness is focused on the dead.
- **Depression** is hopelessness, the loss of happiness, and sadness that's pervasive in all life. It's actually easier than you think.



Grief

- After the **loss of a loved one** (a major stressor) there are two reactions.
- **Grief** is a **normal reaction** that **doesn't impair** normal functioning and will **improve spontaneously** - though it may progress to depression.
- Onset can be anything, and, especially on the test, **duration must be < 12 months**.
- It is important to let the griever grieve, but also always be cognizant of the potential for suicide.
- Grief is **hopeful** and usually **waxes and wanes**.
- The patient **CAN be happy** with family and friends and **CAN** see the future.
- Any depressive symptoms are focused at **the deceased** – anhedonia, depressed mood, spontaneous crying.
- Even psychotic like features – talking **TO** the deceased, maintaining **rituals** as if the deceased is present – if there **IS INSIGHT** (there isn't psychosis), even that is normal. **Do not TREAT guilt** – but you can offer therapy sessions to get them through it.

> ***Things that say "grief only"***
>
> *- Ability to have fun / be happy with family*
>
> *- NO psychotic features, or if they sound psychotic, then there IS insight*
>
> *- Any depressed mood revolves around the deceased or things that involved the deceased*
>
> *- Happiness is possible*

Depression

- Conversely, depression is **pathologic** - often **impairing function** - and won't resolve on its own.
- Using **duration** of symptoms doesn't work anymore (PCBD makes it less useful).
- In depression, the mood symptoms are there, but there has been a transition away from the deceased, and the symptoms have become **pervasive in the patient's life**.
- Depression is **hopeless**, is **PERVASIVE** in multiple elements of life, and does NOT wax and wane.
- The patient **CANNOT** be happy with family and friends, and **CANNOT** see the future.
- If there's any evidence of **psychotic features** (lacking insight), then **the diagnosis immediately becomes depression with psychotic features**; it can't be Grief or PCBD.
- Treat depression with SSRI or SnRIs, ensure to contract for safety, and screen for suicide.

Things that say "this is depression"

- Depressed mood all the time

- YES psychotic features or NO insight

- Depressed mood is pervasive in elements of life beyond those that included the deceased

- Happiness is impossible

- Hopelessness, despondent

Persistent Complicated Bereavement Disorder

- If there's **mostly depression** but the emphasis remains **focused on the deceased** (it's NOT pervasive in all their life), or the duration has exceeded 12 months but they don't meet depression criteria, call it PCBD.
- Treat PCBD with SSRI or SnRI just like depression.
- PCBD is either **persistent** (>12 months) or **complex** (hopelessness, persistent depressed mood) but it's NOT pervasive into all elements of a patient's life.
- PCBD is almost never the right answer on the test because it's fairly ambiguous.

Adjustment Disorder after loved one dying

- By definition, AD can't be in the setting of bereavement.

Post-Traumatic Stress Disorder after loved one dying

- PTSD can occur if the death of the loved one is violent or tragic.
- PTSD will focus on flashbacks, avoidance, and fear rather than on depressed mood.
- On the test, it will either be "obviously PTSD in a violent death" or "obviously depression with a non-violent death."

Post-Partum Differential

- The birth of a child can be a fairly stressful event.
- So stressful that is can **produce mood symptoms**, or more often **reveal underlying psychiatric predisposition**.
- To form a differential and therefore know how to intervene, look at the **timing**, **severity** of symptoms, and **mom's feeling about baby**.
- It's especially important to keep a close eye on a patient who has a history of post-partum psychiatric illness or those beginning to exhibit symptoms.
- Bring a patient back for **close follow-up**.
- The goal's to prevent mom from **hurting herself or baby**. Because there's a gradual **descent into disease** (there's no "switch") it may be possible to detect and prevent potential tragedy.

	Baby Blues	***Post-Partum***	***Post-Partum***
	Baby Blues	***Post-Partum Depression***	***Post-Partum Psychosis***
Baby	# 1 Cares about Baby	> #1 Doesn't care about baby, may hurt baby	> # 1 Fears the baby, likely to kill it
Timing	Onset and Duration within 2 weeks	Onset within 1 month duration ongoing	Onset within 1 month Duration Ongoing
Depression	Dysthymic	MDE	None
Psychosis	None	None	⊕
Treatment	Nothing	Anti-depressants	**Mood stabilizers or Antipsychotics**

Kubler-Ross Stages of Death and Dying

- Everyone deals with death of a loved one or even their own dying process in a different way.
- There are **five stages** typically encountered that may progress in **any order, skip around,** or go **back and forth** between them.
- It's not just an academic exercise to decide which stage a patient is in; it's useful to anticipate reactions and decide what tone or stance to take with the patients.
- On the test, it's pretty easy to spot which stage someone is in. In life, it takes a significant amount of emotional intelligence to get it right.

Denial
Depression
Bargaining
Anger
Acceptance
DDBAA (repeating) or DABAD (palindrome)

	Grief	PCBD	Depression
Onset	Any	> 6 months	Any
Duration	< 12 months	≥ 12 months	≥ 12 months
Focus - **Dysphoria** - **Guilt** - **Anhedonia**	Deceased	→	Pervasive Global
When mood	Waxes and wanes Imagine Happy	←	Persistent Cannot Imagine Happy
Behaviors	Talking TO Praying AT Rituals As if there "Glimpse in crowd" + insight	←	Hallucinations Auditory – WITH Visual – SEE Psychotic Features No Insight
Why considering Suicide	Deceased	→	Negative Self, Despondent, Hopeless

OCD + RELATED DISORDERS

- Obsessive-Compulsive and Related Disorders share the same common thread of an irrational, **anxiety-provoking** thought or need that can only be alleviated by doing a particular **anxiety reducing** action or ritual.
- We use obsessive-compulsive as the model for pathology and treatment for the rest, hence why we spend the most time on it.
- The others are simply categorized by their predominating obsession and compulsion.
- The goal is to control the anxiety (the compulsion) or displace the compulsion to something innocuous.

Obsessive-Compulsive Disorder

- Patients have **persistent, intrusive, unwanted thoughts** (the **obsessions**) that provoke anxiety.
- The only way to relieve these obsessions is by **performing repeated behaviors or mental acts** (the **compulsions**) that neutralize the anxiety.
- The patient is **painfully aware** of the actions/thoughts and how **irrational** they are; they'll often seek help.
- Frequent distress (at least one hour a day) is required for the diagnosis.
- Obsessive-Compulsive disorder is a disorder when function becomes impaired: social interactions, academic performance, or job performance.
- **Psychotherapy (CBT)** is better than medications in treating OCD.
- Therapy is directed either at controlling the anxiety associated with the obsession (desensitization) or redirecting the compulsion to something innocuous that also reduces the anxiety.
- It's a chronic anxiety disease, so treatment with **SSRIs** can be a useful adjunct (TCAs, specifically clomipramine, are also shown to work, but rarely is the right answer on the test). BZDs aren't for OCD – use them only in panic attack.

Obsessive-Compulsive Disorder

Obsession	*Compulsion*
Contamination	Cleaning
Symmetry	Order/Counting
Safety	Lock Checking

The CBT used is Exposure and Response Prevention (ERP)

Clomipramine is the TCA of choice

SSRIs have lots of evidence, SnRIs have less

Hoarding Disorder

- Patients have distress about the thought of losing items and therefore are **unable to get rid of possessions**, regardless of their value.
- These patients often have cluttered homes with a lifetime of accumulated possessions that may compromise quality of life or safety (fall risk, inability for emergency personnel to maneuver around objects, etc.). The cluttering may be so pervasive that it includes trash and or animal hoarding.

Body Dysmorphic Disorder

- Patients are disproportionately preoccupied with **perceived defects or flaws in physical appearance**, concerned they're unattractive or deformed.
- Focus usually centers on flaws of skin (acne), hair, nose, breasts, or **asymmetry** of the body.
- In response to these concerns, patients excessively **check their appearance in a mirror**, engage in repetitive grooming, make comparisons or **seek reassurance** about their appearance. Age of onset is during adolescence; many patients may resort to cosmetic surgery.
- **Muscle dysmorphia**, (mostly in males), comprises a subset of patients preoccupied with insufficient musculature, resulting in patients using anabolic steroids or excessively weightlifting and exercising.

Trichotillomania

- Patients **pull out their hair** to reduce anxiety.
- If a patient has **alopecia** we generally don't jump to psych.
- But if it's hair in **different lengths** (vs a **patchy alopecia**) then it's strongly suggestive of trichotillomania vs medical disease.

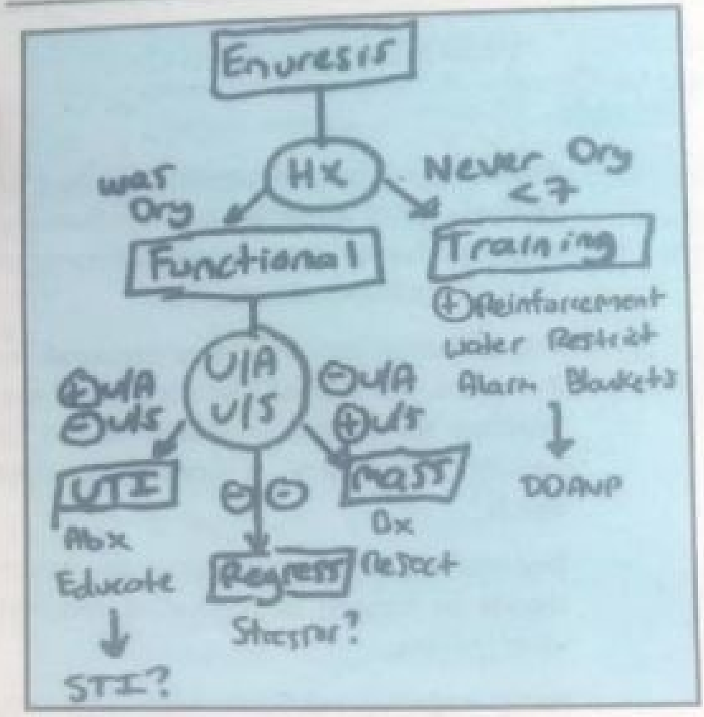
- Take steps to rule out hair loss disease (fungus in particular).
- If she presents with a **small bowel obstruction** as well, think of a **trichobezoar** (a hair ball).

Disorder	***Obsessions***	***Compulsions***	***Effect***
Hoarding	Distress about thoughts of ridding possessions	Retaining useless items: Trash, Trinkets	Unsafe Home
Body Dysmorphic Disorder	Perceived defects in physical appearance ♀	Appearance Checking Reassurance	Excessive cosmetic surgery
Muscle Dysmorphia	Preoccupation with muscle size ♂	Anabolic Steroids Excessive Exercise	Rhadbo Roid Rage "Copper"
Trichotillomania	Non-specific	Hair Pulling r/o Fungus	Hair in Different lengths Bezoar

PEDS BEHAVIORAL

Enuresis

- **Enuresis** is repeated urination in bed or clothes, either intentional or involuntary, and not due to medications, disease, or structural abnormalities.
- The definition is at **> 2 times per week** for **3 months** in a patient that's **> 5 years old**. Wetting the bed, commonly tested in pediatric psychiatry, is **normal up until age 7.**
- Bed wetting **if never dry** until age seven should be treated as normal; it requires toilet training.
- **Avoid negative reinforcement** (shaming, yelling, reprimanding).
- Utilize **only positive reinforcement** (reward and support when doing well).
- Start with **nighttime fluid restriction** and **water alarm blankets**.
- Medications that reduce urinary volume such as **desmopressin (DDAVP)** – start here – or medications that reduce urinary voiding (**oxybutynin**) can be used as an adjunct.
- Last line are TCAs such as imipramine.
- If bed-wetting occurs **after a dry period** then something is wrong.
- This may be **regression** following a stressor (new sibling, sexual abuse), or it could be a **medical / anatomical** problem (like an infection).
- Screen for abuse, educate proper wiping techniques for girls, and screen for a UTI.
- Any STI in a child is confirmation of sexual abuse.



Encopresis

- This is repeated defecation in inappropriate places, either intentional or involuntary, not secondary to a medical condition, medication, or anatomic abnormality.
- To qualify, it has to happen **> 1 per month for 3 months**.
- Treat with toilet training.
- If there's a cognitive impairment, diapers may be the only solution.

Conduct Disorder

- Conduct disorder is **antisocial personality disorder** in a **kid**.
- Look for features that demonstrate a disregard for the rights of others.
- These are the **bullies** who **pick fights** or **destroy property**.
- The biggest tipoff is the **killing or torture of animals**.
- Other criminal behavior **(lying/stealing)** can be seen.
- Unfortunately, this is likely to progress to antisocial personality disorder.
- Attempts at correction should be made as soon as possible with **juvenile detention**, **big brother programs**, or other behavior modifiers.
- If you read the questions as **"antisocial"** but then it's an **adolescent**, it's Conduct Disorder.

Conduct Disorder

Dx	At least 3 symptoms in the past 12 months of violating rules, rights of others, or social norms as follows
Aggression to people or animals	Bullying, threatening, fighting, using weapons, cruelty, forced sexual activity
Property Destruction	Fire setting or other Deceitfulness or theft Broken into other's property, Lies or cons others
Rules Violations	Truancy or disobeying family rulesstaying out at night before age 13 Run away at least twice
Onset	May have onset before or after age 10; many patients also have ADHD

Oppositional Defiant

- A kid who **confronts authority** (parents, teachers) by **yelling** or **throwing tantrums**, but does **NOT break laws** and does **NOT hurt others** is likely oppositional defiant disorder.
- These youths are irritable and argumentative.
- What separates this from conduct disorder is the critical **interaction with peers**.
- They fight, yell, kick, and scream at authority but play well and interact socially with peers.
- Family education and intervention is important, as this condition often progresses to conduct disorder.

Conduct	***Opposition***
Breaks Laws	∅Breaks Laws
Harms Animals	∅Harms Animals
Bullies Others	Bullies Others
Lies + Steals	Lies + Steals
Defiant to Authority	Defiant to Authority

PEDS NEURODEVELOPMENT

Intellectual Disability Disorder

- DSM-V eliminated **Mental Retardation** (MR) from our vocabulary.
- The term has been banned by federal mandate, **"Rosa's Law."**
- MR has been replaced by Intellectual Disability Disorder (IDD).
- This disorder consists of deficits in **cognitive skills** and **adaptive functioning**, occurring during development.
- It's adaptive deficits, not IQ that determines severity: mild, moderate, severe, and profound. IQ scores can still provide a general index, yet a patient can have an IQ above 70 (3 standard deviations from mean) and still be considered to have an intellectual disability. There are multiple etiologies, including **chromosomal** (Down's, Fragile X, cri-du-chat) and **acquired** (maternal substance abuse in utero, maternal hypothyroidism in utero, lead poisoning,).
- Incidence is higher in males. For genetic causes, **prenatal screens** and **genetic counseling** are critical. But don't start a prenatal screen unless mom is willing to terminate.
- The best thing to do in a patient with IDD is begin immediate **education** and **social skills training** once it's identified. Since there's no cure, all we can do is support the patient with IDD and their families.

Severity	***IQ***	***Relative Age***	***Adaptive Function***
None	>70	------	Advanced Life Skills Works ADLs
Mild	50-70	10 (6th grade)	~~Advanced Life Skills~~ Works ADLs
Moderate	35-49	6 (3rd grade)	~~Advanced Life Skills~~ ~~Works~~ ADLs
Severe	20-34	3	~~Advanced Life Skills~~ ~~Works~~ ~~ADLs~~
Profound	<20	1	Total Care

Autism Spectrum Disorder

- ASD is more broadly defined in DSM-5; it's now truly a spectrum from mild forms with limited impairment, to severe forms with impairment early on. There's **no link to vaccines** of any kind.
- There does seem to be genetic predisposition, however, and males are more commonly affected.
- There are **no diagnostic tests,** though some tools have been created to assist in the diagnosis.
- There must be two things: Impaired social communication and restricted repetitive behaviors.

Autism		***ID***
Repetitive		∅ Repetitive
↓ Cognition		↓ Cognition
↓ Social Interactions		**Socially Aware**
↓ Language		Intact Language
IQ Impaired		IQ Impaired

- **Impaired social communication** is manifested as the inability to reciprocate emotionally (understand the value or meaning of an object or event to another person), difficulty using or interpreting nonverbal cues, and failure to maintain relationships. This is manifested earliest as a **failure to meet developmental milestones** such as the social smile, eye contact, parental bonding).

> *There's NO LINK AT ALL between Autism and Vaccines*
>
> *Asperger's is now part of the Autism Spectrum*

Autism Spectrum

Severity	*Age Dx*	*Presents as*
Mild	4-6	Regression
Moderate	2-4	Plateau
Severe	0-2	No Progress

- **Restricted Repetitive Behaviors** are manifested in **stereotyped movements** or speech such as whole body rocking, lining up of objects, **insistence on sameness** (the inability to deviate from routine), and **preoccupation** with particular objects or interests.
- The severity of ASD changes based on the age it's first noticed. The more severe the impairment the earlier it will manifest, and the more care will be required. **Treatment** is focused on **adaptive behaviors** and social integration.

Feature	*Deficit – ASD LACKS*
Impaired Social Communication	Social reciprocity (emotion, empathy) Nonverbal communication (gestures) Social relationship development Joint attention (doesn't care to share)
Restricted repetitive behaviors or interests	Stereotype Behaviors Insistence on Sameness Restricted Interests Altered Sensory Perception

Rett syndrome

- Occurs almost exclusively in **girls** who **regress after a period of normal development until around 6 months.**
- Over time it progresses to death.
- Genetically inherited, give **genetic counseling** to the parents.
- On a test, if you see "young girl" and "maybe autism," choose Rett's.

ADHD

- ADHD is a **disorder** of Attention Deficit (**inattention**) and Hyperactivity (**impulsivity**).
- Essentially, it's a kid who **can't focus**.
- The diagnosis is clinical, but is laborious to list.
- Look for a **trouble-maker** who's disruptive and easily distracted in class.
- Parents and teachers often notice the disorder – **poor grades** in school and **behavioral complaints** from the teacher. But then it turns out it's more distraction than bad behavior.
- To be diagnosed, consider the time, **inattention** symptoms, and **impulsivity** symptoms.
- The onset must be before **12 years old**, have a duration of **> 6 months**, and occur often enough to impair function.
- The inattention is manifested as failing, making careless mistakes, becoming **easily distracted** and or **not being able to follow through** on plans – chores or homework.
- Impulsivity is manifested as **excessive fidgeting,** difficulty **taking turns**, or **interrupting others**.
- These symptoms must also occur in more **than one setting** – home and school.

- There isn't a diagnostic step; it's a clinical diagnosis.
- Treatment is with **stimulants / amphetamines** such as methylphenidate or other amphetamine combinations.
- Avoid stimulants at night to prevent insomnia.
- Help the parents with patient **education** on the disease and how to handle the rambunctious child.
- Finally, the child may need **special classes**; they CAN learn, but lack of focus prevents getting decent grades.
- If you see a question about a "bad kid" and you see anything about seizures, look for absence seizure diagnosis and management.

Impulsivity	Interrupting others, cannot wait turn Blurts out answers Excessive fidgeting, inability to sit still
Inattention	Fails to finish tasks Easily distracted Multiple incomplete tasks
Time	Duration > 6 months Onset < 12 years Frequency enough to impair function
Location	≥ 2 settings
Treatment	Amphetamine Stimulants for kid Parenting for parents Special classes
Follow-up	Absence seizures - EEG - Carbamazepine

Specific Learning Disorder

- Patients may have isolated performance difficulties with reading, spelling, or math. These students perform **substantially below expected for their grade**, measured by standardized testing.
- Possible explanations may also be medical **conditions** (ID, Deaf, Blind, Non-English Speaker) or a display of poor education to date. Therapy to correct medical conditions, **remediation, special education**, or simply a better student to teacher ratio may improve performance.
- Always choose **hearing** or **vision exam** – don't go crazy and start with the basics.

Tic Disorders

- Tourette's Disorder is associated with **OCD** and **ADHD**, having an onset **< 18**.
- The patient has motor and vocal tics for at least **a year**.
- These may be simple and hidden (**hair flicks, blinking, rubbing**) or obvious (**vocal**).
- Vocal tics rarely involves swearing, but rather mostly incomprehensible noises, like grunting or clearing throat.
- Treat with **dopamine antagonists (antipsychotics)** and **habit reversal therapy** (behavioral).
- Look for an "ADHD" kid who gets put on **stimulants**, which then **worsens Tourette's**.

Childhood-Onset Fluency Disorder (also known as stuttering)

- It has an unknown etiology and unknown therapy.
- It's repetition of syllables, words, or phrases that interrupts normal speech.
- Speech therapy can help; children also often grow out of it.

PERSONALITY DISORDERS

Introduction

- Personality disorders are **rigid, permanent,** and **maladaptive** traits that define the way a person behaves.
- These traits become embedded **early in adulthood** and are completely **ego-syntonic**.
- They're engrained and patients don't see it as a problem.
- Thus, it's almost impossible to treat them.
- Instead, the goal is to learn how to interact with them.
- Remember, you can't diagnose an **adolescent** with a personality disorder (they might grow out of it), though the traits can be spotted early on.
- Be able to identify qualities and be aware of how to interact with them. Generally, treatment is long-term psychotherapy; it's largely unsuccessful.

CLUSTER A

1) Paranoid:

   - Patients are **mistrustful, suspicious of others,** and usually interpret benign behaviors as malevolent.
   - They'll use **projection** as a defense mechanism.
   - They'll be **isolated** and may have **short-lived delusions** of persecution that'll interrupt their lives, but rarely persist.

2) Schizoid:

   - Detached **"loners"** who **don't interact** and are **happy in isolation.**
   - They don't experience emotions like others.
   - Think of the IBM employee with an office under the stairs or a midnight shift toll-booth operator.
   - They usually don't need treatment as they **avoid everyone** - including the clinic.
   - Their logic is they don't get in trouble so why get therapy?

3) Schizotypal:

   - Everything is **bizarre**.
   - It looks like schizophrenia by their dress, logic process, and actions.
   - They don't have **hallucinations**, but do have **magical thinking** (lucky charms, extreme superstition).

> *If ever a patient SOUNDS like they have a personality disorder but it isn't affecting their lives in any appreciable way, they're said to have "Cluster Traits."*

CLUSTER B

4) Borderline:

   - The patients teeter on the border of psychosis.
   - This personality disorder has many associations.
   - They often complain of **emotional numbness** - committing **suicidal gestures** (like cutting).
   - They're **impulsive** and often engage in **prematurity** and **drugs**.
   - These are the patients who **attempt suicide** to get attention, and if poorly timed, can **succeed**.
   - They also have **rapidly changing moods**: anger, happiness, sadness that **change on a dime** (much faster than a rapid cycler or bipolar).
   - They frequently exhibit **splitting**.
   - They can be treated with dialectic behavioral therapy – it's a form of cognitive behavioral therapy that now has a test-association with Borderline.

5) Histrionic:

- Patients are **attention-seeking** with **excessive contrived emotion**, **over-the-top** action and dress, and **hypersexuality**.
- They use their physical appearance to be seductive and behave very **theatrically**.
- Those patients do poorly in a mid-life crisis as their looks begin to fade – they'll feel that no one cares about them anymore.
- It's very similar to narcissistic.
- *Look for the hypersexual, overly dramatic woman with that needs to be the center of attention*

6) Narcissistic:

- These patients are **all about themselves** – they express **delusions** of their **own importance**.
- They also dress over-the-top, but as to draw attention to themselves.
- They're often **exploitive** and **self-consumed** so they ignore the needs to others.
- They're special and so demand the **best for themselves**, carrying a sense of entitlement.
- Frequently it's a sign of insecurity as they're often **jealous of others**.

(Above and below are stereotypes. The tests love stereotypes, so don't blame me)

Look for overly well dressed, self-centered men who don't need to be the center of attention because obviously they already are.

7) Anti-Social:

- The real bad boy of cluster B.
- They have **no regard for rights of others**, are **impulsive**, and **lack remorse**.
- These are society's criminals.
- Often preceded by **conduct disorder**, this is the only personality disorder that absolutely can't be diagnosed prior to 18.
- At 18, conduct disorder becomes antisocial.
- You can't and **shouldn't treat** them; it just makes them better liars. Often, incarceration is the only option.

CLUSTER C

8) Avoidant:

- These patients are shy, **fearing criticism**, and saddled with a **feeling of inadequacy**.
- They **desperately want friends** but avoid them for **fear of rejection**.
- They'll often pass on promotions or choke during presentations because they're afraid of failing and/or being judged.
- These folks will come see you for help. Avoid power struggles, make patients choose.

9) Dependent:

- Patients are **submissive, clingy**, and generally **need to be taken care of**.
- They'll rely on others to make decisions and won't initiate projects or conversations.
- Because of their **unrealistic fears of isolation**, they'll often go to great lengths to save a relationship.
- They'll also generally obey a stronger voice.

10) Obsessive-Compulsive:

- There's going to be a **preoccupation** with **orderliness** and control at the **expense of efficiency**.
- These patients have difficulty **meeting deadlines** and **finishing tasks**.
- They're rigid, but despite their failures are ego-syntonic.

	PD	Description	Examples	How to handle them
A	Paranoid	Distrustful, suspicious, interpret others are malicious	Gene Hackman, *"Enemy of the state"*	Clear, honest, nonthreatening
	Schizoid	Loners, have no relationships but also are happy not having any relationships	Night-Shift Toll Booth	You won't see them
	Schizotypal	Magical Thinking, borders on psychosis, Bizarre Thoughts, Behavior, and Dress	Lady Gaga	Brief Psychotic Episodes Clear, honest, nonthreatening
	Borderline	Unstable, Impulsive, Promiscuous, emotional emptiness, unable to control rapid changes in mood, suicidal gestures	*"Girl Interrupted"* *"Fatal Attraction"*	Suicidal Gestures may be successful Splitting, Dialectic Behavioral Therapy
B	Histrionic	Theatrical, attention-seeking, hypersexual, use of physical appearance, dramatic, Exaggerated but superfluous emotions	*"Gone with the wind"* Marilyn Monroe	Set rules, insist they are followed
	Narcissistic	Inflated sense of worth or talent, self-centered, fragile ego, uses eccentric dress to draw attention, demands special treatment	*"Zoolander" Ron Burgundy*	Set rules, insist they are followed
	Narcissistic	Inflated sense of worth or talent, self-centered, fragile ego, uses eccentric dress to draw attention, demands special treatment	*"Zoolander"* Ron Burgundy	Set rules, insist they are followed
	Anti-Social	Criminal. No regards for rights of others, impulsive, lacks remorse, manipulative. Must be >18 years old (conduct disorder)	Tony Soprano The Joker	Jail, Set rules, insist they are followed
	Avoidant	Fears rejection and criticism, wants relationships but does not pursue them, Passes on promotions	*"Napoleon Dynamite"* Shy hot Librarian	Avoid power struggles, make patients choose
C	*Dependent*	Unable to assume responsibility. Submissive, *clingy, fears being alone*	Stay at home mom in an abusive relationship	Giver clear advice, patient may try to sabotage their own treatment

	Obsessive-Compulsive	Rigid, orderly perfectionist. Order, Control. Perfection at the expense of efficacy	*"Monk"*	

PHARM: ANTI-DEPRESSANTS

Anti-depressants

- The theory behind depression is the **monoamine hypothesis** that basically says, ***"you don't have enough neurotransmitters, that's why you're sad."***
- In particular, focus has turned to **serotonin** and **norepinephrine**.
- There are multiple mechanisms but they all result in one unilateral outcome - **increased neurotransmitters** leading to elevation of mood. But because we know **maximal effect happens 3 weeks later**, it must be more than just an increase in the concentration of neurotransmitters. This has led to the concept of **plasticity** – happy neurons tend to become easier to stimulate. Then. applying more stimulation leads to long-term mood elevation, with a potential ability to come off the medication.
- Finding the right drug / dose combo is more **trial-and-error** than science. The goal is to get on the maximum tolerable dose and stay on it. A patient (and you) should give a drug a chance. Unlike other diseases in medicine, you really need to give medications **longer than you feel is proper** to see if they work. Plasticity takes time. That means giving a drug at least **> 6 weeks** and **maximum dose** before switching. Once one that works for the patient is found, treat the disease for **> 6 months** to stabilize and avoid relapse.
- If there has to be a switch, allow a **> 3 week washout** period to avoid potentially dangerous compound effects. We say ***"666" (6 weeks at a dose, 6 months at maximum tolerable dose, 6 week washout)*** as the advanced organizer in the video to help you remember it. They're all ranges, and with cleaner medications serotonin syndrome isn't as much a concern – even when combining SSRIs.
- **Selective Serotonin Receptor Inhibitors** (SSRIs) are generally **clean** and used **1st line**, but are known for their side effects: **decreased libido** (some don't want sex), and or **delayed ejaculation** (used illicitly to prolong sexual intercourse – they obviously want sex). Serotonin syndrome (discussed in the catatonia lesson) is a rare side effect when medications are given without washout.

- *SSRIs are escitalopram, fluoxetine, paroxetine, sertraline.*
- *Say this 10 times.*

- **Serotonin and Norepinephrine reuptake inhibitors** (SnRIs) should be seen as "better SSRIs." While more evidence exists for SSRIs (they've been around longer), the SnRIs tend to be more expensive versions of SSRIs with less side effects. Their efficacy should be considered identical to SSRIs.

- *SnRIs are desvenlafaxine and duloxetine. Say this 10 times.*

- The only **Atypical** you need to know about is **bupropion**. Never used in bulimics (causes seizures), it's the "wonder drug" that helps with **smoking cessation**, treats depression, and **prevents weight gain**. Choose it when smoking cessation is the comorbid disorder you want to treat.

- ***There is one atypical: Bupropion***

- **Serotonin Modulators** are generally not great anti-depressants, but have hidden benefits in their side effect profile. **Mirtazapine** can be used as an appetite stimulant for someone malnourished and depressed. **Trazodone** is used as a sleep aid, not for depression at all **(beware priapism).**

- ***Mirtazapine is an anti-depressant and appetite stimulant***
- ***Trazodone is used for sleep, not depression. Priapism.***

Anti-Depressants

SSRIs	(Es)citalopram Fluoxetine Paroxetine Sertaline	**↓ Libido** sometimes **Delayed Ejaculation** sometimes Serotonin Syndrome GI, Insomnia
SnRIs	(Des)Venlafaxine Duloxetine	Cleaner, better versions of SSRIs. More expensive
Atypical	Bupropion	**Smoking cessation** No weight gain Bulimia NEVER (↑ seizures)
SM	Mirtazapine Trazadone	**Appetite Stimulant Sleep Aid, Caution priapism**
TCAs	"-tryptilines" Imipramine Desipramine Doxepin	Used for **enuresis** (anti-ach) 1st line use is **neuropathic pain** Can be **Lethal** because of CCC: (Convulsions, Coma, Cardiac) so get an ECG Has **Anti-Ach** properties (dry mouth, sedation, Uretention, Constipation)
MAO-Is	Phenelzine Tranylcypromine Selegiline	**HTN Crisis** when mixed together, lack of washout or eating of **tyramine** (red wine/cheese) Distinguish from other hypertensive-hyperthermia disorders in psych by the ABSENCE of lead-pipe rigidity and fever

Bad Classes

- The following medications are included for completeness and because these are the ones the test will use to trick you. The answers will be more on side effects than on intended use; these classes are generally NOT USED for depression anymore.

Anti-Depressant RULES
• **> 6 weeks trial**
• **> 6 month of treatment**
• **> 3 weeks washout**
• **Max the Dose**

- **Tricyclic Antidepressants (TCAs)** have anticholinergic side effects. They're used to treat neuropathic pain and enuresis more than depression. They're never the right answer, though questions still come up about their **cardiac toxicity** (they'll widen the QRS complex and lead to arrhythmias), the **convulsions** (they cause seizures), and **coma** (altered mental status).

- ***TCAs are the tryptilines, (des)ipramine, doxepin. Say it 10 times.***

- **MAO-I** are never the right answer either. There's no reason toever go near these meds now. The only thing that might be asked revolves around the **hypertensive crisis** when used at the same time (this is really why there's a washout period, even though we don't use these meds anymore) or when consumed with **tyramine** (red wine, cheese). This is separated from the catatonia hypertensive disorders by the absence of fever, absence of lead pipe rigidity, and because you see an antidepressant you don't recognize.

- ***MAO-is aren't worth remembering. Selegiline and Phenelzine. 10 times.***

MOOD STABILIZERS

Mood Stabilizers

- There's been a major change in the way Bipolar disorder is taught. We give the high yield info first, then talk about the real-to-life changes you'll see on the wards that are still grey, but big enough to warrant the extra time on.

Mood Stabilizers

Lithium	**First-Line, Drug of Choice** Bipolar, Acute Mania, Depression Augmentation	**Teratogen** **Nephrotoxic > 1.5** Causes Nephro DI Narrow TI
Valproate	**First Line** in Bipolar if Li cannot be used	**Teratogen** (Spina Bifida) Thrombocytopenia Agranulocytosis
		Pancreatitis
Quetiapine	**Second Line** bipolar All phases of treatment	Weight gain QTc prolongation
Lamotrigine	**Second Line** bipolar Newer anticonvulsant	Blurred Vision SJS
Carbamazepine	Third line bipolar Trigeminal Neuralgia Absence Seizures	**Teratogen** (Cleft palate) Rash, SJS AV Block

What you need to know?

- **Lithium** is the best drug for treating bipolar / mania.
- It is, however, the **worst drug** to be on.
- It has a **narrow therapeutic index** and causes **nephrotoxicity.**
- This leads to **nephrogenic diabetes insipidus** (hyponatremia) and (over time) renal failure.
- It can also cause a host of complaints that are ambiguous such as nausea, vomiting, and abdominal pain.
- Finally, it's a **teratogen;** its utility is limited in women with bipolar who are either wanting pregnancy or those who do not accept contraception.
- When using lithium, **lithium levels** can assess for compliance and safety.
- **Valproic acid** is still **first line,** but it's used **if lithium can't be.**
- In reality, it's an arbitrary choice between lithium and Valproate.
- Valproic acid is also a teratogen, causing **spina bifida**, and therefore has the same limitations on women that lithium had.
- Valproate is a much more tolerable drug.
- Untested side effects are in the table.

- **Quetiapine** has made headway in the treatment of mania and bipolar. It has **sedating** side effects, making it ideal for those in mania. It can cause weight gain. It can also cause **QTC prolongation**, so ensure an ECG is obtained.

Treatment by Phase

Depressed	*Manic*	*Maintenance*
Mood Stabilizers: Quetiapine Lurasidone	**Mood stabilizers:** Lithium Valproate Carbamazepine	**Mood stabilizers:** Lithium Lamotrigine
Combo Olanzapine/Fluoxetine	**Antipsychotics:** Quetiapine Olanzapine Aripiprazole Risperidone Ziprasidone Chlorpromazine	**Antipsychotics:** Same as manic phase

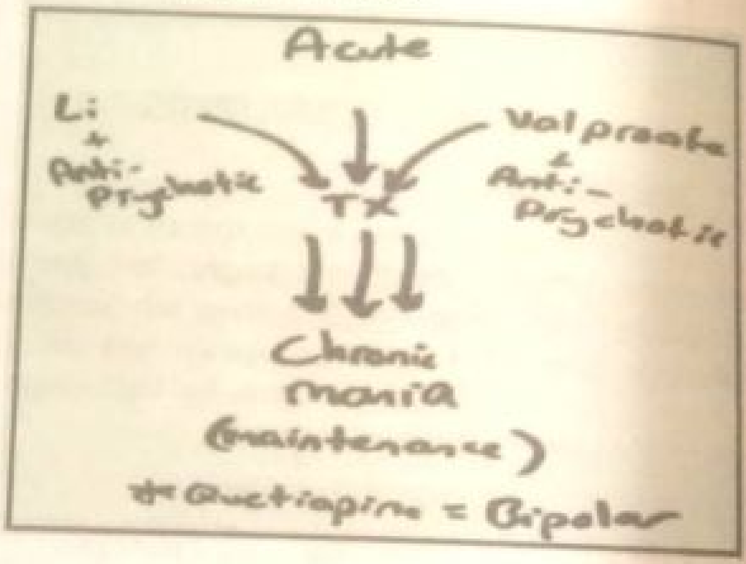
- **Lamotrigine** used to be after valproate on the hierarchy. It's cleaner than the rest, but is now considered 2nd line.
- **Carbamazepine,** formerly considered to be the same and indistinguishable from Lamotrigine, is now third line. It shouldn't be used for bipolar or mania. Instead, use it for **absence seizures** and **trigeminal neuralgia.**

e Real Deal

- There are three phases of bipolar treatment: the **manic phase,** the **depressed phase**, and the **maintenance phase.**
- Previously, the goal was to be on as few medications as possible to avoid toxic side effects.

The new thinking is to subdue the mania, then **keep the patient on the medications** that allow control of mania.

- This flip is not prevalent, but gaining ground – increase the risk of side effects early to ensure control of the disorder and not have to escalate later.
- This is knowing scaling back can occur if side do effects occur.
- **Quetiapine** can used in **all phases** of treatment, making it very attractive.
- **Valproate** and **Lithium** are usually used in mania and maintenance only.
- Lamotrigine is now seen as a medication for maintenance only.
- In general, **avoid antidepressants** in treating bipolar, as that will precipitate a manic episode. A test favorite is the major depressive episode that's treated with SSRI, then presents in mania. That's Bipolar I - not MDD.



ANTI-ANXIETY

Anti-Anxiety Medications

- The take away is that the more **chronic the anxiety** the better it will respond to **psychotherapy.**
- The more **acute the anxiety** the more it will respond to abortive therapy such as **benzodiazepines.**
- Along the spectrum there are many disorders related to anxiety.
- Though they aren't categorized as being similar, anxiety shows itself in many

forms: **impulse control**, **OCD**, and **OCD-related disorders**. It's even present in PTSD and other stress-related disorders.

- The right answer for the chronic pervasive diseases is **psychotherapy.** If medications are going to be used, the **SSRI** is likely to be the right choice almost all the time. SSRIs are discussed in Psych Pharm I: anti-depressants. Never use benzos to treat chronic anxiety.
- ***Anti-Anxiety***

Benzos	Abort panic attack Treats EtOH withdrawal	Dependence Withdrawal Seizure
SSRIs	First-Line long term medication for treatment of chronic anxiety: OCD, PTSD, GAD	See Anti-Depressants. Ø useful in acute attack
β-Blockers	Performance Anxiety	Bradycardia, Asthma

> *A "b52" is an alcoholic shot with 3 ingredients.*
>
> *A B52 is also a bomber plane in the US Air Force.*
>
> *A B52 is an intramuscular injection (a "shot") with 3 ingredients: haloperidol, lorazepam, and diphenhydramine.*
>
> *It "bombs" the patient into sedation. It's always the wrong answer on the test because it counts as chemical restraints*

- For acute panic attacks, we use abortive agents such as **benzodiazepines.**
- Benzos should be used to treat acute attacks only, as dependence and tolerance can occur. Benzo withdrawal is the same as alcohol withdrawal and can be life threatening. This is discussed further in the substance abuse disorder lesson. **CBT** can also be useful for aborting attacks with learned behaviors, but usually doesn't control spontaneous attacks.
- The test loves to ask about **public speaking** as a **specific phobia**. Use **Beta-blockers** as needed before a big engagement. Practicing (effectively CBT with desensitization) is also helpful. Beta blockers can lower HR and cause depressed mood, but since they're only being prn this becomes less of an issue. Just know the association.

Chronic Anxiety

GAD	Psychotherapy > SSRI SSRI adjunct ~~BZD~~
OCD	Psychotherapy > SSRI SSRI adjunct ~~BZD~~
PTSD	Psychotherapy > SSRI SSRI adjunct ~~BZD~~

Acute Anxiety

Panic Attacks	BZD
	Psychotherapy
	SSRI

ANTI-PSYCHOTICS

First Generation Antipsychotics = Typical Antipsychotics

- Excess **dopamine** in the **mesolimbic** pathway is responsible for the positive symptoms of psychosis – hallucinations, delusions, and disorganized thought.
- Historically, the first created medications went after positive symptoms. Because they were historically first (when we didn't know about receptor subtypes), they were **non-selective dopamine antagonists**. The stronger the antagonism, the better they worked on the positive symptoms. The problem, however, is that since they aren't specific they also block dopamine in other places.

This means the stronger the antagonism the worse the side effects.

- Blocking **dopamine** in the **nigrostriatal tract** can lead to Parkinsonism and the **extrapyramidal symptoms**. Blocking dopamine in the **tuberoinfundibular tract** causes gynecomastia (by disinhibiting prolactin, effectively ↑ Prolactin).
- And because they're nonspecific, the better they are at positive symptoms (**potency**), and the higher the **EPS** side effect profile. Interestingly, there's an **inverse relationship** between potency and **Anti-cholinergic** side effects.
- These early antipsychotics are now called **First Generation Anti-Psychotics** (FGA). They've traditionally been referred to as **Typical** antipsychotics.
- **Haloperidol** is the **most potent**, and so has the highest incidence of **EPS**. It's no surprise then that it's often used acutely to subdue combative patients, not as chronic therapy. Other FGA / typicals in descending order of potency are: fluphenazine, thioridazine, and chlorpromazine.

Typicals = First Generation Antipsychotics (FGA)

Haloperidol *Fluphenazine* *Thioridazine* *Chlorpromazine*	Mesolimbic D2C-R-I treats positive symptoms	Potency of drug proportional to EPS
	Nigrostriatal Antagonism leads to EPS side effects	Potency inversely proportional to Anti-Ach
	Tuberoinfundibular antagonism causes ↑ prolactin, gynecomastia	

- Atypicals = Second generation Antipsychotics (SGA)

Risperidone *Quetiapine* *Olanzapine* *Aripiprazole* *Ziprasidone*	Both **D2$_C$** and **5-HT$_1$** so work on ⊕ and negative sxs More selective so lower risk of EPS Currently "first line" for Psychosis	QTc **prolongation** EPS, Gynecomastia, Sedation, Anti-Ach (small risk) **DM** and **Weight Gain**

- **Clozapine**

Unique to itself	The **best antipsychotic** The most selective for **D$_2$C** and **5HT$_1$** (positive and negative) Drug of last **resort**	**Agranulocytosis** Requiring CBC q week

Second Generation Antipsychotics = Atypical Antipsychotics

- Eventually, drugs got better. Specifically, we went after the **D2c-R** in the **mesolimbic tract** to improve symptom control while reducing side effects. Second generation antipsychotics (SGA), also called Atypicals, also target the negative symptoms by antagonizing **5-HT1 Serotonin Receptors.** These made for cleaner drugs with less chance of EPS.
- For all comers, Atypical Antipsychotics are the drugs of choice for treating psychotic disorders. The thing to watch out for with atypicals is **QTc prolongation** (obtain an ECG prior to starting and after finding a stable dose). These medications

have reduced potency as well. For all intents and purposes they're identical to each other. Associate **quetiapine** with **drowsiness** (good for mania and psychotics features), and **olanzapine** with **DM** and **weight gain**.

Clozapine, a Class of its own

- The first atypical, **Clozapine,** was best in class.
- It is hands down, the **best atypical ever made.**
- It's highly receptor-specific, has no extrapyramidal side effects, and treats both positive and negative symptoms. It's perfect.
- Except that it kills people. **Agranulocytosis** was so common that in order to use it, there must have been an exhaustion of all other medications; it's used as a medication of **last resort only.**
- Those who are put on it require **weekly CBCs** and registration with federal agencies to monitor its use.
- It's the **most effective**, the **most dangerous,** and the **drug of last resort.**
- Attempts to make a safer Clozapine have resulted in the other atypicals.

Choosing the Right Medication and Dose

- **Dosing** is easy; titration can be done **daily**.
- Simply choose one, increase the dose until there's control of the psychotic disorder and stay on it. If the dose is maxed and there's no control, try another.
- **Medication selection** can be harder. Formulations, potency, and side effect profiles dictate which medications get used in which situations.
- For **routine compliant** patients, any **Atypical Antipsychotic** will suffice. You shouldn't be asked to choose between them, except maybe for the Quetiapine or Olanzapine called out above. These medications are **oral**.
- **Intramuscular** forms such as Haloperidol or olanzapine can be used in an emergency. **Oral dissolving tabled – ODT -** (quetiapine, risperidone) formulations can be used in noncompliant patients where either IM isn't available, or a less potent antipsychotic is required.
- **Depot** forms (olanzapine, risperidone) are used for chronic noncompliance. Don't forget **Clozapine.**

Choosing the Right Drug

Compliant Young Adult, without Complications	Any atypical po	↓ SE profile
Combative ER Patient	Haloperidol Depot	Sedating
Noncompliant Psychotic	Olanzapine depot Risperidone depot Haloperidol depot	q 1wk
Dysphagia or IM not available	Olanzapine ODT Risperidone ODT	Oral dissolving tablet
Hospitalized and off their meds	Atypical, ↑ **Dose q Day** until maxed, then try another	

Extrapyramidal Side Effects (EPS)

- **Akathisia** is a **subjective** feeling of **restlessness** or the urge to move.
- It's treated by **decreasing the dose**. Other options include beta blockers and **anti-ach** medications such as Benztropine.
- **Acute Dystonia** is a reversible condition of involuntary muscle contractions: typically hand ringing, torticollis, and **oculogyric crisis** (the patient gaze is locked in one direction as in going down stairs they

can't look down). It can be reversed with **anticholinergic** medications such as **benztropine** or diphenhydramine.

- **Dyskinesia** comes from inhibition of the nigrostriatal tract. Too much dopamine can result in psychosis. Too little dopamine yields **Parkinsonism** (dyskinesia) - treat with **anti-cholinergics** or specific dopamine-agonists (**benztropine**).
- The major worry of these drugs is **tardive dyskinesia**. It's a late onset, **irreversible** condition of temporarily suppressible oralfacial movements caused by **dopamine-receptor sensitization.** You blocked it, but the brain says "I need it!" so the brain does it with more receptors. You can only stop the drug (increasing dopamine to a sensitized system only further sensitizes the system), which initially **worsens symptoms**.

Extrapyramidal Side Effects

Akathisia	A **Feeling of Restlessness**	↓ Dose.... Beta blockers Anti-Ach (Benztropine)
Acute Dystonia	Involuntary muscle contractions, hand ringing, torticollis, and **oculogyric crisis**	Anti-Ach (Benztropine)
Dyskinesia	**Parkinsonism** Dyskinesia = Bradykinesia	Anti-Ach (Benztropine)
Tardive Dyskinesia	Irreversible **hypersensitization** of dopamine-R = suppressible **oral-facial** movements	Stop Drug. Sxs **initially worsen**

PSYCHOTIC DISORDERS

Introduction

- A **delusion** is a **fixed false belief.**
- To the patient it's a glaring universal truth - one that can't be denied.
- To the rest of the world there's no sound basis whatsoever.
- Delusions often **can't be confronted,** so it's best not to try.
- Put another way, the patients **have no insight**.
- In dealing with delusion disorders it's critical to identify the **duration** of symptoms, and how **bizarre the delusion / illogical the thought process**.

Delusion	Fixed false belief that could be true
Bizarre	Fixed false belief that could not
Delusion	Possibly be true

Because this "bizarre" modifier may vary based on cultural belief, it is no longer so heavily used.

Schizophrenia

- Schizophrenia is a **thought process disorder** with an unknown etiology.
- There's definitely a **genetic component,** while **overload of dopamine** (confirmed) and **serotonin** (likely) contribute to a constellation of thought symptoms culminating in the final diagnosis.
- Schizophrenia typically presents **in young** adults (**20s**) following a major life stressor (**college**) with a **psychotic break**.
- A normal healthy person suddenly snaps, acts bizarrely, and hopefully gets on meds.
- Rule out **drugs** (illicit).

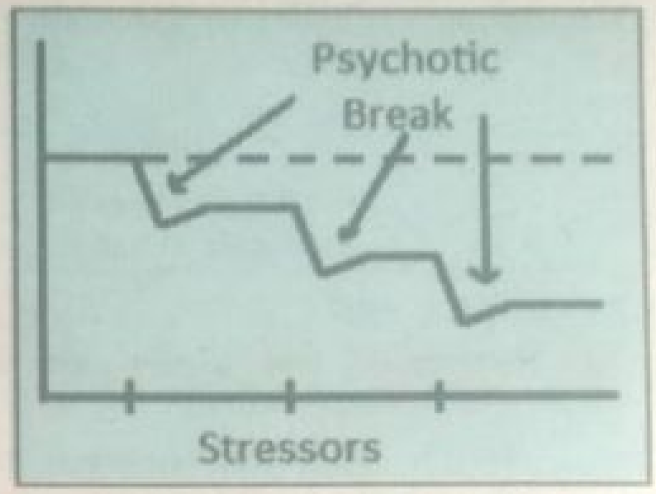
- Once diagnosed, schizophrenia is a lifetime of relapses with continually **declining mental functioning** each break.

DSM-V says

- Any **two** as long as **one** is from items 1-3.

- Treatment is with **anti-psychotics**. They come in two forms. The first-to-be-made aka the first-generation, but second-line treatments are **typical antipsychotics** focused primarily on the positive symptoms, targeting dopamine-receptor antagonism.
- Typical antipsychotics are stratified by potency, but often have a larger side effect profile.
- **High-potency typicals** (haloperidol, fluphenazine) have a stronger effect, but higher incidence of **extrapyramidal symptoms**, while low-potency typicals (chlorpromazine) have high rates of **anticholinergic** side effects.
- The last-to-be-made aka the second generation, but first-line treatments are **atypical antipsychotics**. They're better, cleaner drugs that treat both positive and negative symptoms. The risk of EPS and anti-cholinergic side effects are less, but often potency is weaker.

Schizophrenia	
⊕ Sxs	1. Bizarre Delusions 2. Hallucinations 3. Disorganized Speech 4. Disorganized or catatonic behavior
⊖ Sxs	5. Flat affect, cognitive defects, poverty of speech, anhedonia



The subtypes of schizophrenia (Disorganized, Catatonic, and Paranoid) are no longer a thing. You can modify schizophrenia with mood symptoms or with catatonia.

Brief Psychotic Disorder and Schizophreniform

- If shortly after a severe event – any major stressor can do it – psychotic features appear, we call it brief (or acute) psychotic disorder.
- The **onset > 1 day** with a **duration < 1 month.**
- BPD can progress to schizophreniform.
- Post-partum psychosis is brief psychotic disorder that occurs in response to pregnancy.
- If handled acutely, the duration shouldn't progress into schizophreniform ranges – treatment is usually < 1 month.
- Schizophreniform is longer than BSP, but not as long as Schizophrenia. The **duration** is **1< to <6** months.
- Treatment is longer - about **3-6 months.**

Schizophrenia by Duration and Modifiers

Brief Psychotic Disorder	Duration > **1 dy** and < **1 mo**
Schizophreniform	Duration > **1 mo** and < **6 mo**
Schizophrenia	Duration > **6 mo**

Schizoaffective	schizophrenia and mood - MDE - Mania
Delusional	Non-Bizarre Delusions, no other symptoms, and generally functional

Schizoaffective Disorder

- Schizophrenia may present with or without mood symptoms.
- When there are **no mood symptoms** - it's only psychotic – it's schizophrenia.
- When the **mood symptoms** are present, but psychotic predominate, it's schizoaffective.
- If **mood symptoms predominate** with a little psychosis, it's a mood disorder with psychotic features. See the spectrum. Learn the schizoaffective.

Tx	⊕ Sxs	Typical	Haloperidol, Thiazide, Chlorpromazine
	⊖ Sxs	Atypical	Risperidone, Quetiapine, Olanzapine, Ziprasidone, Aripiprazole
	Best		Clozapine

Delusional Disorder

- The **delusions** are fixed, false beliefs but are **non-bizarre** (not true, but believable).
- There's a **logical thought process** and everything they say is legit (except the delusion).
- There's no loss of function, but the delusion may cause legal or relationship trouble.
- Treatment is **gentle confrontation over years of psychotherapy** - no drug will do.

PTSD + RELATED DISORDERS

Stress Disorders (PTSD and ASD)

- These occur when something really bad **(the stressor)** either directly happens to the patient, or is witnessed by them.
- These stressors cause bad reactions, which we define as the **disorders here.**

PTSD = Post-Traumatic Stress Disorder

ASD = Acute Stress Disorder

RAD = Reactive Attachment Disorder

DESD = Disinhibited Social Engagement Disorder

AD = Adjustment Disorder

- ***The stressor*** itself involves **exposure** to **actual** (others) or **threatened** (self) **death, serious injury** (combat), sexual violation **(rape)**, or **child abuse**. The stressor "counts" if the exposure occurred either through **direct experience** (happened to self), was **witnessed in person** (happened to others), or even by **learning of something happening to a loved one.** The other way the stressor "counts" is if someone is exposed to **repeated** or **extreme exposure** to aversive details (first-responders picking up body parts, detective investigating child abuse).
- ***The Disorder is harder*** to characterize. There are five categories, each with their own symptoms.
    - **Intrusive** symptoms are things that happen that shouldn't – memories, flashbacks, nightmares.
    - **Negative mood** resembles depression, and if you take any of the depressive symptoms, it counts.
    - **Dissociative symptoms** such as amnesia or depersonalization (see that lesson later).
    - **Avoidance** symptoms are literally that – avoiding memories, symbols, locations, or even conversations about the event.

  - **Arousal** symptoms involve hypervigilance, irritability, easily startled, and lack of concentration.
- Timing:
  - If symptom duration is **> 1 month,** it's classified **Posttraumatic stress disorder.**
  - If the duration is **> 3 days,** but **< 1 month,** it's **acute stress disorder (ASD).**
- Treatment:
  - **Group therapy** is the definitive treatment. Early implementation (even prophylactically) reduces duration and may limit the disorder to ASD.
  - Failing to address the disorder extends the symptoms into PTSD. **SSRI/SNRIs** are the preferred medications.
  - While benzodiazepines can be prescribed for panic attacks, they're easily abused. Further, PTSD is predominated by long-term anxiety, not panic attacks.
  - **Cognitive behavioral therapy** (flooding, desensitization) can be used, similarly to the way we described in OCD.
  - **Mood disorders** (depression, anxiety) and **substance abuse** disorders are quite common comorbidities.

PTSD and ASD

Pa:	**Stressor** - Actual Death - Threat Death - Combat - Rape - Abuse	**Exposure** - Experienced (Self) - Witnessed (strangers) - Learned (family) - Repeated exposure to effects
Pt:	**Disorder** - Intrusion - Neg Mood - Dissociation - Avoidance - Arousal	Nightmares, Flashbacks, memories Depression-like Depersonalization, amnesia Symbols, locations, memories Hypervigilance, irritability, easily startled, CHANGE concentration
Dx:	> 3 days AND < 1 month duration = Acute Stress > 1 month duration = Post-Traumatic Stress	
Tx:	Group Therapy (best) SSRI/SNRI (adjunct) Benzos (panic attack only) CBT	
F/u:	Mood Disorder Substance Abuse Disorder	

Reactive Attachment Disorder

- When the stressor is **neglect** or **abuse** during **infancy and childhood**, a child's ability to pair, bond, or attach to adults may become impaired.
- The condition is evident before **5 years old** and Autism spectrum has been ruled out.
- If they **attach to everyone** (inappropriately), it's called DSED.
- If they **fail to attach to anyone** it's RAD.
- Treatment is often not targeted at the patient, but instead to the **caregiver**, by coaching good parenting skills.

RAD/DESD

Pa:	Stressor = Neglect or Abuse in infancy
Pt:	Disorder = too much attachment (DSED) too little attachment (RAD)
Dx:	<5 years old r/o Autism
Tx:	Caregiver – parent coaching / teaching
F/u:	Mood disorder Learning disabilities

Adjustment Disorder

- When the stressor is **less severe** (marital strife, losing a job, nonviolent death of someone close) the reaction is less severe.
- Adjustment disorder is changes in mood (depression), anxiety, or conduct.
- It should **start within 3 months** of stressor and **duration** should be **less than 6 months** after the event.

AD

Pa:	Stressor = Non-life-threatening event - Marital strife, loss of a job, moving away
Pt:	Disorder = Mood changes that don't quite fit for another mood disorder
Dx:	Begin < 3 months from stressor Lasts < 6 months from stressors
Tx:	Generally not needed (reassurance only)

SLEEP DISORDERS

Obstructive Sleep Apnea

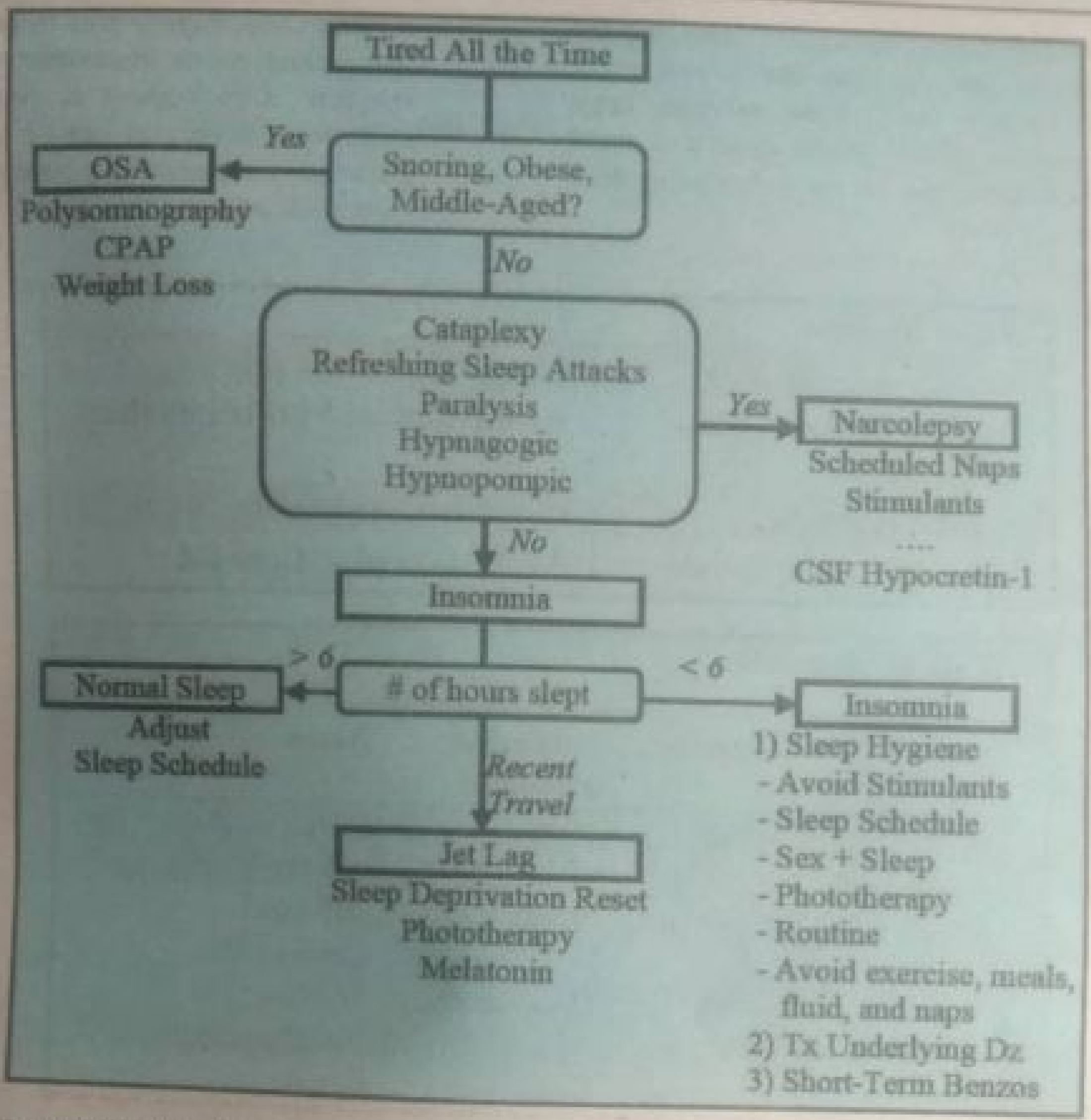
- Sleep apnea is the arrest of sleep because of excess body habitus. Patients will be **obese**, have a **short neck** and a **difficult-to examine oropharynx**.
- The major complaint will be **daytime somnolence.**
- Ask the roommate (usually spouse on test) if they **snore**.
- If he does, send him for a **polysomnography**, commonly called a sleep study.
- OSA is diagnosed by **15 obstructive apneas / hour** OR **5 apneas / hour** AND snoring or breathing pauses with daytime somnolence.
- These people need to **lose weight** and get a **CPAP** at night to keep the airways open.
- Reducing night time hypoxemia can avoid the resultant **pulmonary hypertension** that can lead to **isolated right heart failure.**

Central Sleep Apnea

- It's possible to have **central sleep apnea** in a thin person – treat with BiPAP with backup vents.
- These patients have lost their intrinsic drive to breathe spontaneously.
- This may be related to opiates or idiopathic.
- Also look for Cheyne-Stokes respirations (though this is not pathognomonic, on a sleep question this respiratory pattern is the buzz-word for CSA).

Narcolepsy

- Narcolepsy is a sleep disorder whereby the patient is **rapidly plunged to REM sleep** (sleep attacks) that happen **at least 3 times per week for 3 months** - a one-time event doesn't count.


Tired All the Time
Snoring, Obese, Middle-Aged?
Yes
OSA
Polysomnography
CPAP
Weight Loss
No
Cataplexy
Refreshing Sleep Attacks
Paralysis
Hypnagogic
Hypnopompic
Yes
Narcolepsy
Scheduled Naps
Stimulants
....
CSF Hypocretin-1
No
Insomnia
> 6
# of hours slept
< 6
Normal Sleep
Adjust
Sleep Schedule
Insomnia
1) Sleep Hygiene
- Avoid Stimulants
- Sleep Schedule
- Sex + Sleep
- Phototherapy
- Routine
- Avoid exercise, meals, fluid, and naps
2) Tx Underlying Dz
3) Short-Term Benzos
Recent Travel
Jet Lag
Sleep Deprivation Reset
Phototherapy
Melatonin

- The patient will suffer these sleep attacks, seemingly spontaneously, though often they can be induced with a startle (laughter, loud bang).
- **Cataplexy** is the loss of muscle tone while conscious. As the person goes out they go limp; they may be **paralyzed on waking**.
- While commonly associated with narcolepsy, both **hypnaGOgic** (when GOing to sleep) and **hypnopompic** hallucinations (on waking up) can be experienced by anyone.
- People are going to nap so it's best to **schedule naps** and use **stimulants** to keep them awake (amphetamines).
- **CSF hypocretin-1** is a new diagnostic step for Narcolepsy.

Insomnia

- Defined as the **difficulty falling asleep** or waking up too early without the ability to fall back asleep. This must happen **3 nights a week for 3 months** to meet criteria. When a patient complains of insomnia, the first step is to determine the **number of hours** of sleep; if a patient sleeps **6-8 hrs** just **adjust sleep time** or investigate for **OSA**.
- After ruling out sufficient sleep, just not when they want to sleep, the next step is to consider their sleep hygiene.
- Sleep hygiene revolves around these principles: **Avoid stimulants** (caffeine, cocaine) five hours before sleep, establish a **sleep schedule** (programming the brain to sleep at a certain time), use

phototherapy (lights out = sleep), use the bed for **sex and sleep** (don't read, watch TV, etc in bed), **avoid exercise, large meals**, and **fluid** before sleep and **avoid naps** during the day (to ensure being tired at bed time).

- If fixing sleep hygiene fails to correct, or the patient needs immediate relief (on the test, sleep hygiene is always first), short term sleep aids can be used (see potency, addiction potential, and contraindications to the right).

Sleep Hygiene

Bed for sleep and sex	Lights out = sleep only
Avoid stimulants 5hrs before sleep	Avoid exercise 5 hrs before sleep
Stop taking naps	Avoid food and fluids
Develop sleep schedule	Avoid alcohol as sleep aid

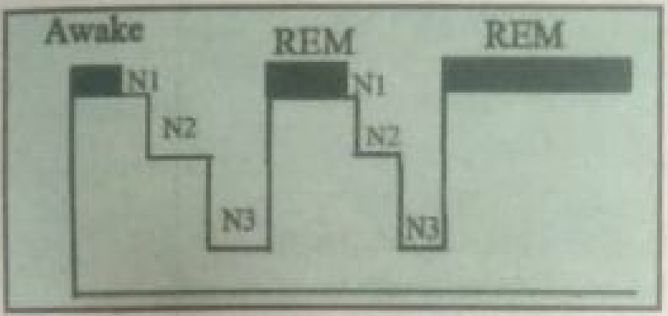
Sleep Medications

Drug	***Potency***	***Addictive Potential***	***Notes***
Diphenhydramine	Weak	None	Don't give to elderly
Quetiapine	Moderate	None	Off-label Cardiac QTc
Trazodone	Strong	Dependence	Erection, Nasal congestion
Zolpidem	Strongest	High	Benzo

PHYSIOLOGY OF SLEEP

Stages of Sleep

- The **sleep stages** are defined by **EEG** and **EMG** patterns.
- Restful sleep is achieved by Rapid Eye Movement (**REM**) **sleep**.
- All other stages are considered Non-REM sleep.
- Where there used to be 5 stages, there are now 4, with stage III and IV being combined into Non-REM Stage 3 (N3). To progress to the next stage of sleep, one must pass through the previous (N1→N2 →N3→ REM). The longer one sleeps, the longer REM periods become, while the shorter the other stages become (more **restful sleep** the longer you **stay asleep**). When near the top of the graph (**N1, N2**, REM), aka nearer to awake, the **easier it is to arouse**.
- **Sleep latency** is the time from going to bed to falling asleep. It's **elevated in insomnia** and **decreased** in **sleep deprivation**.
- **REM Latency** is the time from falling asleep to REM sleep. It has an average of **40 minutes**, meaning **naps aren't restful**. This can be **shortened** by **depression** or **narcolepsy** (narcolepsy patients go straight into REM, causing **cataplexy**).
- **REM Rebound** occurs when the body has been deprived of REM. It's easier to get REM and you get more of it.



Stage	*EEG*
N I	Theta Waves, Absence of Alpha
N II	K-Complexes, Sleep Spindles
N III	Delta
REM	Awake EEG, Atony, Saccadic Eyes, Erections

Neurotransmitters of Sleep

- The neurotransmitters of sleep can be remembered by the mnemonic **SAND**.
- They're the order in which sleep stages occur.
- It's useful for predicting how drugs will affect sleep and why certain drugs are given to aid with sleep.
- Other things that can impact sleep are **benzos, barbiturates**, and **EtOH**.

Neuro	*Effect*	*Drugs*
Serotonin	↑ Sleeps	Melatonin, Tryptophan
ACh	↑ Dreams	
Norepi	↑ Dreams	Cocaine / Stimulants
	↓ Wakes	
Dopamine	↑ Wakes	Antipsychotics (sleep more) Bromocriptine (arousal)
GABA	↓ Stage 4	Benzos
	↓ Sleep Latency	(not more than two weeks)
Other	↓ REM	EtOH
	REM Rebound	Barbiturates

Parasomnias

- Parasomnias are the disorders that occur during sleep.
- Focus on two things here; be able to **diagnose** a parasomnia and reinforce how **drugs influence** the sleep cycle.
- **Nightmares** are **dreams gone bad**. They can occur in any age group and occur during **REM sleep**. They'll frighten or startle a person from sleep. Generally, they're recalled upon wakening. Focus should be on dealing with stressors that bring them on, but because they're within REM they can be treated with things that reduce REM. PTSD patients who experience flashbacks in nightmares may use **EtOH** to reduce them, when what they need is group therapy and an **SSRI**. Generally, pharmacotherapy should be avoided.
- **Night Terrors** present in **little boys** who "wake up" and go frantic - **screaming in terror** but **remember nothing** of the event. Parents are the ones who need counseling as the kid could care less. He **sits up** - he has muscle tone so it can't be REM. Night Terrors occur in stage **N3**. They generally require no treatment (**reassurance**), but N3 sleep can be decreased with benzos – DON'T DO THIS.

	Nightmares	*Night Terrors*
Stage	REM	N3
Memory	+ Remember	Ø Remember
Tone	No tone (in REM)	Maintains Tone screams, yells goes back to sleep
Treatment	If part of PTSD, treat PTSD, otherwise address stressor	Reassurance to parents

- **Sleep talking** is just that; the patient has **incongruent speech** during sleep. It does not require intervention. Oh, and the patient never reveals secrets.
- **Sleep walking** can also be sleep eating, sleep having sex, or sleep driving a car. This is bad. It worsens with **BZD1 use.**

SOMATIC SYMPTOM DISORDERS

- Somatic symptom disorders are hard to deal with. They're defined by a **real somatic complaint** but **without organic cause.** The symptoms should be considered **real**; they're certainly felt by the patient, even in the absence of objective findings. It's for this reason that we also discuss factitious disorder and malingering - conditions in which people are "doing it to themselves."

Disorder	*Sxs*	*Preoccupation*	*Motivation*
IAD	None	Acquiring illness	Unwanted
SSD	Somatic	Somatic Sx	Unwanted
Conversion	Neurologic	None + Stressor	Unwanted
Factitious	Any	Fulfilling Sick Role	Intentional
Malingering	Any	Secondary Gain	Intentional

- The motivation and conscious effort are relevant. By itself, the presence of unexplained medical conditions doesn't warrant the diagnosis. It's the individual's thoughts, feelings, and behaviors surrounding these symptoms that are major factors.
- These are often associated with depression or anxiety (the chicken and egg have not yet been determined). Even if you DON'T find anything wrong, remember that the patient's pain is real.
- The **motivation**, **preoccupation**, and **presence of clinical findings** separate the diseases of this section. All of them (except malingering) require **psychotherapy** with regular **medical follow-up**.
- Clear boundaries should be set – what will and will not be ordered, how frequent visits can be, etc. Patients should have a **single, dedicated provider** who can prevent unnecessary use of resources, but

also screen for the development of new complaints (which may not be somatoform but rather a real new condition).

Illness Anxiety Disorder

- Defined as an **excessive preoccupation** and anxiety directed at **acquiring a serious illness** for **6 months**, but without somatic symptoms.
- ***The primary difference between somatic symptom disorder and illness anxiety disorder*** is that in SSD there's a somatic complaint, whereas in IAD there isn't. The anxiety of SSD is over the somatic complaint, whereas the anxiety of IAD is over potentially getting a disease. **Despite reassurance** IAD patients will seek multiple providers, get unnecessary tests, and spend excessive time looking for explanation of minor symptoms, blowing them out of proportion to their true cause. There are no symptoms, therefore the symptoms are not intentionally produced, the motivation is subconscious, and the disorder is egodystonic.
- The anxiety is over potentially acquiring a disease.

DSM-IV Correlate: Hypochondriasis renamed. The preoccupation with an illness, usually manifested as acquiring that illness, rather than having any particular complaint.

Complaint	*Preoccupation*	*Motivation*
None	Acquiring Illness	Unwanted

Example: Despite multiple negative screenings for cancer, the patient insists she has the cancer and asks for another mammogram

Somatic Symptom Disorder

- There are **1 or more** somatic symptoms **lasting 6 months** or longer without medical cause.
- This disorder is predominated by **preoccupation with a somatic complaint.** There may or may not be a real medical condition behind it.
- If there is, it's a **disproportionate concern** to the severity of the illness.
- These patients are **more often women** and will frequently seek medical attention from **multiple physicians.**
- Common complaints are **pain, fatigue,** and other nonspecific complaints that are often difficult to address.
- There are somatic complaints, the symptoms aren't intentionally produced, the motivation is subconscious, and is ego-dystonic. The anxiety is over the symptoms.

DSM-IV Correlate: Somatization disorder required there be a combination of somatic symptoms of pain, gi, or sexual dysfunction. This requirement is removed. Somatic Symptom Disorder is now defined by the preoccupation with a somatic symptom despite the absence of clinical findings

Complaint	*Preoccupation*	*Motivation*
Pain	Somatic Sx	Unwanted

Functional Neurologic Symptom Disorder (Conversion)

- A patient has a **neurologic complaint** (paralysis, sensory deficits) despite **no organic cause.**
- Often following a major emotional stressor, the neurologic complaint often reflects the stressor. Look for **inconsistencies** in the exam or history.
- **Motivation** (compared to the next two disorders) is crucial – the symptoms of conversion disorder **aren't fabricated.**
- To be sure, often **imaging is required** to rule out a true neurologic complaint.
- Two elements are key to making the diagnosis. Despite having a neurologic complaint that may be severe (blindness), the patient will **not hurt themselves** (will not walk into a wall).

- The second is the **"Bell indifference,"** where despite the overt neurologic complaint, the patient may not worry about the condition.
- While **psychotherapy** can often undo the neurologic damage, treating the disease as its neurologic correlate (physical rehab for a "stroke") often allows the psyche an escape to return to normal without "admitting" there was no deficit to begin with.
- The symptoms aren't intentionally produced, the motivation is subconscious, and the disorder is ego-dystonic.

DSM-IV Correlate: Conversion disorder remains essentially unchanged. Stressor → neurologic symptom. It's the remnant of Freudian teaching – the emotional stress converts into a physical one

Complaint	*Preoccupation*	*Motivation*
Neurologic	None, but Stressor induced	Unwanted

Factitious Disorder (and by proxy)

- A patient can present with any complaint – somatic, neurologic, or otherwise.
- This complaint is **self-inflicted**. There's an **intention to deceive** medical personnel into believing the patient is sick.
- This can be done by causing injury or disease, contaminating lab tests, or in any other way manipulating the diagnosis.

DSM-IV Correlate: Factitious disorder has been renamed – it used to be Munchausen. The Eponym is no longer used.

Complaint	*Preoccupation*	*Motivation*
Any	Fulfilling sick role, Purposeful deceit	Intentional

Example: A mother injects small amounts of fecal material into her daughter's IV line when no one is watching to keep her septic (Factitious Disorder by Proxy)

- Factitious disorder is characterized by the motivation – **seeking to fill the sick role.**
- While this exact nomenclature isn't in DSM-V, it's helpful to differentiate from malingering.
- In Factitious Disorder, the person is seeking attention or fulfilling a role. They may know what they're doing is deceptive, but they aren't doing it for material gain. It requires **confrontation** and (ultimately) **psychotherapy**.
- If a person inflicts illness on another person (a dependent such as a child, intellectually incapacitated adult, or an elder) it's deemed **factitious disorder by proxy**. This constitutes abuse.

Malingering

- Malingering shares all the same elements as Factitious disorder except the motivation.
- The patient is sick because it's **self-inflicted** or they **deceive.** The symptoms are fabricated or self-induced.
- It's intentional; the mechanisms are the same as factitious. However, it's the **motivation that's different**.
- A malingerer is doing it for secondary gain that's more material: collecting insurance, getting out of jail, getting a pardon based on special circumstances, or getting pain medication from an ED visit.

DSM-IV Correlate: Malingering disorder is unchanged

Complaint	*Preoccupation*	*Motivation*
Any	Fulfilling sick role, Purposeful deceit	Intentional, material gain

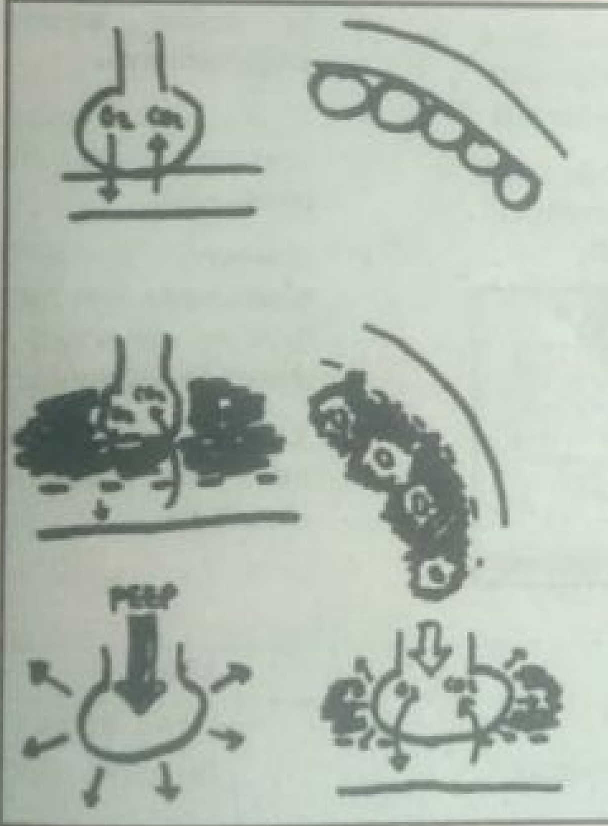
Example: A woman with an abnormal CT scan claims that she has stage IV breast cancer monthly, and asks for symptomatic relief with phenergan and codeine.

PULMONOLOGY

ARDS

Pathogenesis and Introduction

- ARDS is a **non-cardiogenic pulmonary edema** that results from **increased permeability of capillaries** permitting the transudation of fluid from capillaries into the interstitium.
- This causes a barrier to diffusion preventing gas exchange resulting in a **hypoxemia.**
- It looks and feels like CHF but the cardiovascular function is intact, hydrostatic pressures are normal (meaning that the **capillary wedge pressure** is **normal**), and it's the capillary permeability that drives disease.
- Too many leaky capillaries then leads to pulmonary edema and alveolar derecruitment.



Normal gas exchange and no leaky capillaries in the normal state

Impaired oxygenation as a product of increased diffusion barrier from leaky capillaries in ARDS

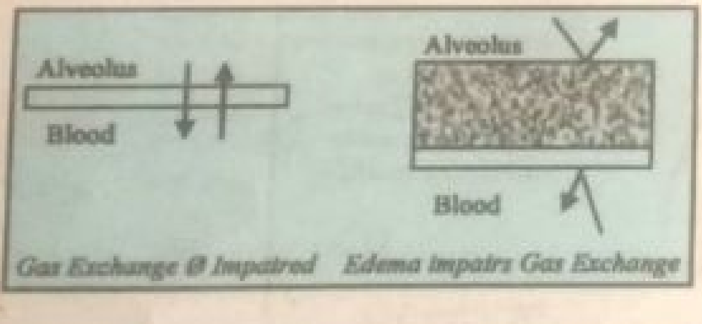
PEEP provides alveolar recruitment and improves diffusion of oxygen by reducing diffusion barrier

Presentation

- This is a patient with **pulmonary edema** (SOB, cough, crackles) and a nasty looking CXR (**bilateral white out**).
- The patient is also one without a reason for CHF (MI, HTN, Arrhythmia, Fluid) and has instead a **really sick presentation** (as in the ICU).
- To cause capillary permeability to increase so significantly requires **GNR septicemia, burns, TRALI,** or **drowning**.
- These patients usually present to the hospital then crash in the ICU, rather than a person presenting in florid pulmonary edema.

Diagnosis

- A patient with a systemic disease and pulmonary edema (especially someone **volume down** or **hypotensive**) is likely enough for the diagnosis.
- A **CXR** will show **white out** bilaterally.
- However, to definitively diagnose ARDS vs CHF a measurement of **capillary-wedge pressures** via a **Swan-Ganz cath** is required.
- This will show a **decreased or normal wedge** (no backup of fluid) and an **increased or Normal LV function** (not heart failure).
- Both findings are in direct contradiction to CHF. Generally, it's not done for CHF (patients aren't sick enough to get a Swan-Ganz), though there are certainly HF patients sick enough to make it to the ICU.
- A patient with ARDS will be intubated, full of lines, and ripe to do the assessment on. A PaO2 to FiO2 ration will be < 200.



Gas Exchange @ Impaired *Edema impairs Gas Exchange*

$$J = K\,[P_{cap} - P_{int}) - (\pi_{cap} - \pi_{int})]$$

Fluid movement across a capillary

ARDS causes ↑ in K, fluid leaks out

PEEP causes ↑ in P_{int}, pushes fluid back in

Treatment

- **Intubation** and **Oxygenation** are crucial as first line therapy.
- With intubation, application of **PEEP** increases the interstitial pressures, forcing the fluid back into the capillaries.
- The vessels remain leaky and only close once the **underlying disease is corrected**.

Monitoring/Complications

- When someone's put on PEEP it's possible to induce **barotrauma** or induce **pneumothorax**.
- If the patient suddenly presents with worsening SOB after PEEP, suspect barotrauma.
- However, if a patient becomes **hypotensive** and has a **mediastinal shift** (tracheal deviation) a **tension pneumo** should be suspected.
- Confirm the diagnosis with a CXR and treat with needle decompression and **chest tube**.

	CHF	ARDS
Exacerbating Factors	HTN, MI Fluid Overload	Sepsis, Burns, Drowning, TRALI
Chest X- Ray	Bi Pleural Effusions Bi Hazy Infiltrates	Total White Out Severe Bi Infiltrates
Capillary Wedge	↑ (25)	Normal (10)
LV Function	↓	Normal
Treatment	Diuresis, Control of HTN, PEEP if severe	PEEP Intubation Tx Underlying Dz

ASTHMA

Introduction and Pathology

- Asthma is a reactive obstructive airway disease caused by an **inflammation** and **bronchoconstriction** that results in increased resistance to airflow.
- It's an allergic disease (Asthma, Allergy, Atopy) and is likewise **IgE / Mast cell mediated**.

Presentation

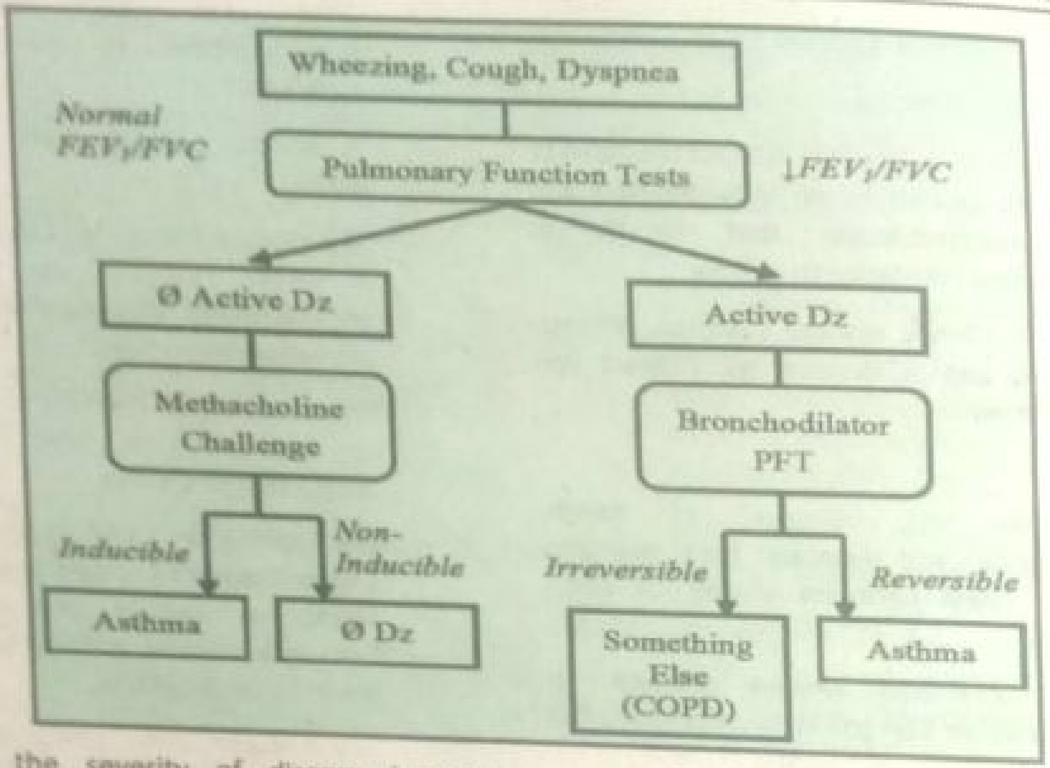
- Patients will complain of **cough**, **wheezing**, and **dyspnea**; they may also claim **chest tightness** during an acute attack.
- The constricted airways produce air trapping; air can get in on inhalation, but can't get out on exhalation.
- Physical exam reveals wheezing and a **prolonged expiratory phase** with a potentially **hyperinflated** or **hyperresonant** chest (an ominous sign).
- Signs of severe dyspnea (accessory muscle use or the absence of lung sounds) signal the presence of **status asthmaticus** - a medical emergency.
- Obtaining a history and physical as well as risk factors is crucial for the decision making that follows.
- Between attacks, the lungs usually sound normal.

Diagnosis

- If someone comes in with an acute onset of wheezing and dyspnea SKIP the diagnosis and move directly to treatment.
- In the **outpatient setting** there are a number of diagnostic modalities, of which **Pulmonary Function Testing** is by far the best.
- If the patient has active airway disease at the time of the test the **FEV1/FVC** will be **decreased**.
- They can be **reversed** with **bronchodilators** to definitively diagnose asthma.
- A normal patient does not rule out asthma.
- A patient suspected of having asthma but a normal FEV1/FVC can be given the **methacholine challenge** test to provoke bronchoconstriction.
- There are other ancillary tests that come up from time to time that may be suggestive of asthma.
- **Eosinophilia** on a CBC or Sputum sample, **Charcot-Leyden Crystals** or **Curschmann's Spirals** on sputum, and **Allergen Skin Testing** are useful, but you should rely on the PFTs for diagnosis.
- Use Allergen Skin Testing when severe, refractory, or to assess which exposures trigger the disease. These tests should not be routinely performed.
- Besides diagnosis, **severity** of disease is a critical element to evaluate as it'll drive patient management.
- It's determined by **frequency of daytime symptoms**, **nocturnal symptoms**, and **severity** of the PFTs.
- They are broken down into steps, or grades, indicating which medications need to be added.

Treatment

- Treatment targets the two elements of asthma: **decreasing inflammation** and **reversing bronchoconstriction**.
- Inflammation is conquered by steroids, bronchoconstriction by beta agonists.
- Then, there are a few drugs that have been added to the mix.
- Patients who have symptoms infrequently can use a **rescue inhaler** (short acting β-Agonists or even Anticholinergics) as needed.


Wheezing, Cough, Dyspnea
Normal FEV₁/FVC
Pulmonary Function Tests
↓FEV₁/FVC
Ø Active Dz
Active Dz
Methacholine Challenge
Bronchodilator PFT
Inducible
Non-Inducible
Irreversible
Reversible
Asthma
Ø Dz
Something Else (COPD)
Asthma

- As the severity of disease increases medications are added.
- **Daily Inhaled Corticosteroids** will decrease the inflammation while rescue inhalers can control the bronchoconstriction.
- For frequent symptoms **Long Acting Beta-Agonists (LABA)** are added to **Inhaled Corticosteroids** (and must NEVER be used on their own).
- From this point, the dosage of steroid increases from low-dose steroids to high-dose steroids, and then to **PO steroids**.

- Bronchoconstriction	Theophylline, SABA/LABA, Leukotrienes
- Inflammation	Inhaled / PO Corticosteroids
- Stabilizing	Cromolyn / Nedocromil

Step	*Daytime Symptoms*	*Nocturnal Symptoms*	*PFTs (FEV_1)*	*Treatment*
Intermittent	≤2 /wk	≤2/month	≥80%	Rescue Inhaler
Mild Persistent	< 1 /day	>2/month	≥80%	Low Dose ICS
Moderate Persistent	≥ 1/day	>1/week	60-80%	Low Dose ICS and LABA
Severe Persistent	≥ 1/day	frequent	< 60%	High Dose ICS and LABA
Refractory	Refractory Severe Persistent			PO Steroids

Treatment Progression

1. SABA
2. SABA + ICS
3. SABA + ICS + LABA
4. SABA + ↑ICS + LABA
5. SABA + ↑ICS + LABA + Oral Steroids

ICS = LTA

Before adding an inhaler, asses to make sure the patient **Knows how to use** and **is using the inhalers correctly.**

- Be aware of other drugs that can be used in place of or in addition to the LABAs.
- The new guys to the market are the **Leukotriene Antagonists.** For all intents and purposes, a Leukotriene Antagonist is an inhaled Corticosteroid and can be used interchangeably. They should not be used together.
- **Theophylline** is a po Adenosine Antagonist. It's pretty old but is still in use. This is never the right answer on the test. It may still be used in patients because of the cost of inhalers, but this is ALWAYS WRONG for your exams.
- For exercised induced asthma with **known triggers** the IgE/Histamine Stabilizers (**Nedocromil** or **Cromolyn Sulfate**) can be used **immediately before known exposure** but with limited use.
- Spend a lot of time on the treatment progression listed to the right, then just know other treatment options exist.

Treatment Progression

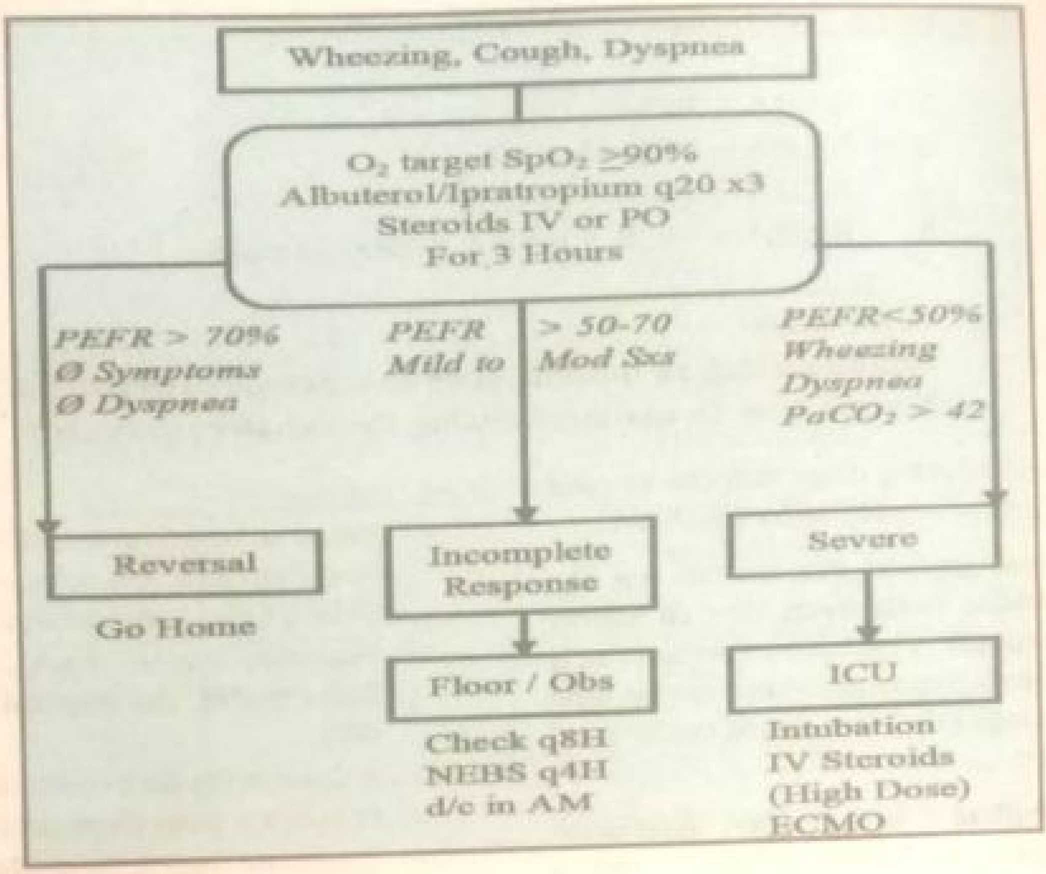
1. SABA
2. SABA + ICS
3. SABA + ICS + LABA
4. SABA + ↑ICS + LABA
5. SABA + ↑ICS + LABA + Oral Steroids

ICS = LTA

Before adding an inhaler, asses to make sure the patient **Knows how to use** and **is using the inhalers correctly.**

Acute Exacerbation

- When someone presents to the ED with acute or refractory symptoms they need to be treated and stratified.
- Evaluation involves **Peak Expiratory Flow Rates (PEFR),** the **Physical Exam**, and an **ABG**.
- A Chest X-ray isn't useful but often done to rule out other causes of dyspnea.
- Treatment begins immediately with **O2, Albuterol/Ipratropium Nebulizers** (to reverse bronchoconstriction) and **corticosteroids** (to reverse the inflammation).
- Peak flow, CO2 retention, oxygen saturations, and lung assessment should be repeated after the initial intervention.
- Rescue therapy for refractory disease involves **Racemic Epinephrine Nebulizers, Subcutaneous Epinephrine,** and **Intravenous Magnesium.** These are added in an attempt to avoid intubation. Ultimately, if there are signs of rising CO2, decreasing pH, or the absence of lung sounds, intubation is required.
- When they first arrive in the ED a Peak Flow should be performed. If there's **no improvement** after **3 hours of continuous nebulizer treatment** they go to the **ICU**; if better (**100% improvement and symptom free**) they go **home**. Anywhere in between gets admitted to the hospital for further management.
- "Further management" really means Albuterol + Ipratropium every four hours with ongoing oral or IV steroids.


Wheezing, Cough, Dyspnea
O_2 target SpO_2 ≥90%
Albuterol/Ipratropium q20 x3
Steroids IV or PO
For 3 Hours
PEFR > 70%
Ø Symptoms
Ø Dyspnea
PEFR > 50-70
Mild to Mod Sxs
PEFR<50%
Wheezing
Dyspnea
$PaCO_2$ > 42
Reversal
Go Home
Incomplete Response
Floor / Obs
Check q8H
NEBS q4H
d/c in AM
Severe
ICU
Intubation
IV Steroids
(High Dose)
ECMO

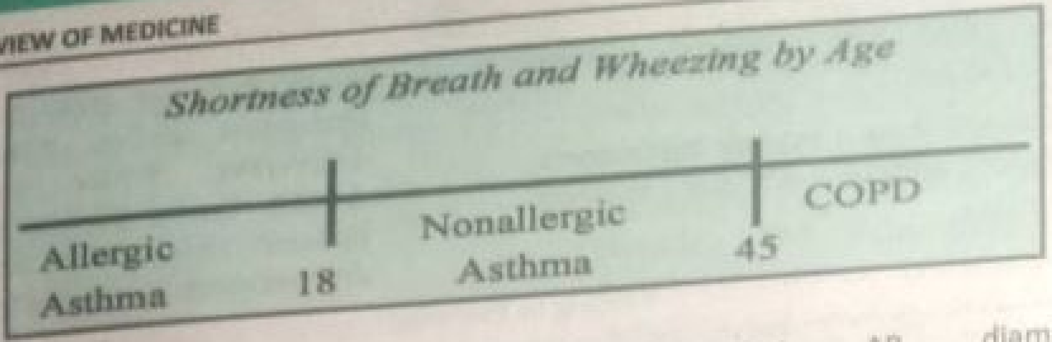
COPD

Introduction

- COPD is a combination of emphysema and bronchitis that produces **airway inflammation** and **irreversible broncho-constriction**.
- The primary cause of COPD is **cigarette smoking**. Because only 20% of smokers get COPD but 90% of COPDers were smokers, there must be other contributing factors: **genetic** (as in α1-AntiTrypsin deficiency) and/or **environmental factors** influence the final disease.
- **Emphysema** is the destruction of **alveolar walls** at the terminal bronchiole (i.e. in the **small airways**) with fibrosis.
- Loss of **elasticity** causes **air trapping** - allowing air in on inhalation while preventing air out on exhalation.
- **Bronchitis** is defined as a **productive cough** for **more than 3 months** in **2** consecutive years
- It's characterized by **mucous production** that obstructs the large airways.
- Together, there'll be **ciliary loss, ↑goblet cells, ↑mucous production**, increased **smooth muscle hypertrophy** (narrowing the airways and ↑ resistance to flow), accumulation of **interstitial inflammatory infiltrates** (causing ↓ gas exchange as a result of decreased diffusional area), and a **loss of elasticity** leading to airwaycollapse during expiration.
- The chronic hypoxia in alveoli leads to an **↑ pulmonary vascular resistance** and subsequent **pulmonary HTN**.

Pathology to Presentation

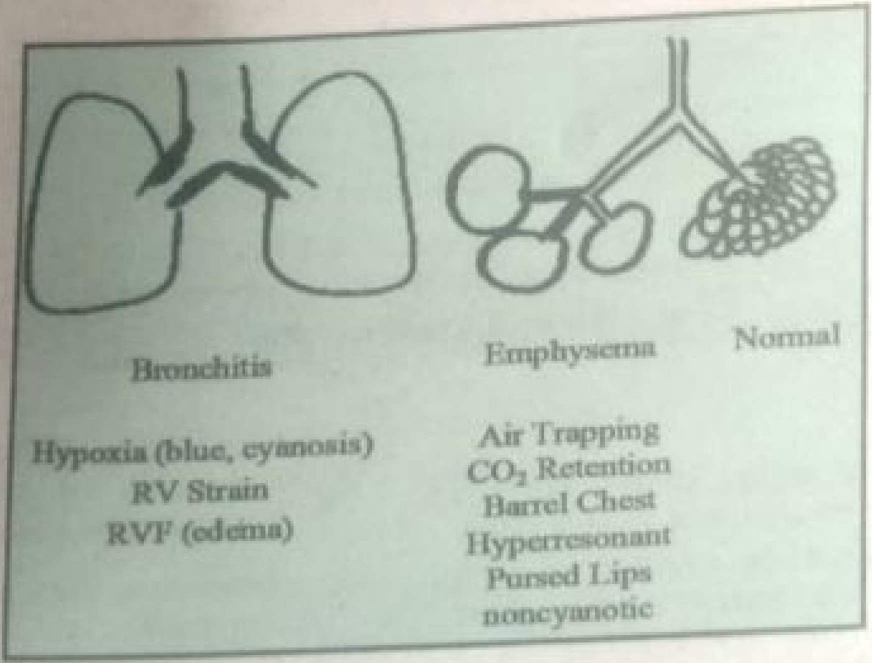
- A patient presenting with COPD will present with wheezing and dyspnea.
- Risk factors for COPD (as opposed to asthma) are **smoking** ~40 pack-year history, **age > 45**, and the physical signs of symptoms of COPD not present in Asthma.



Shortness of Breath and Wheezing by Age

Allergic Asthma
18
Nonallergic Asthma
45
COPD

- With bronchitis the so called ***"blue bloaters,"*** the **chronic cough** combined with the **cyanosis** and **edema** predominate.
- Bronchitis produces hypoxia and the subsequent increase in pulmonary vascular resistance.
- Signs of **clubbing and edema** of the digits indicates chronic hypoxia. The result is **right heart failure** that manifests with **JVD, edema,** and **hepatosplenomegaly**.
- Emphysematics suffer from **air trapping**, which causes the **barrel-chest** of an increased AP diameter and **hyperresonance** on percussion.
- They'll breathe through **pursed** lips to **prolong expiration** and reduce the resistance of airflow out of their lungs. Because it's a struggle to get air out of the lungs the hard work of breathing causes **weight loss** and **accessory muscle hypertrophy**.
- The trapped air reduces expulsion of carbon dioxide.



Bronchitis
Hypoxia (blue, cyanosis)
RV Strain
RVF (edema)
Emphysema
Air Trapping
CO_2 Retention
Barrel Chest
Hyperresonant
Pursed Lips
noncyanotic
Normal

Diagnosis

- The only diagnostic modalities that can diagnose COPD are the **pulmonary function tests**.
- Other tests will be performed as a result of the chief complaint and can be suggestive of the underlying disease. They can also be used to indicate severity of an acute flare.
- The **CXR** will show **flattened diaphragms, translucent lung fields** (both from increased air in the lungs), and a **rotated heart silhouette**.
- The **EKG** might show **RVH** (from cor pulmonale) or a **Right Axis Deviation**

(from RVH or rotation from hyperinflation).

- An **ABG** will show a **hypoxic hypercapnic respiratory acidosis** and is useful to direct treatment.
- Finally, PFTs will show an **irreversible obstructive airway disease: ↓FEV1 ↓FEV1/FVC, ↑↑RV, ↑TLC,** and a **↓DLCO**. Finally, even if there are no outward signs, a **CBC** may show an **erythrocytosis** in response to the hypoxia.

Finding to Pathology

Finding	*Pathology*
Barrel-Chest	↑AP Diameter, Accessory muscle hypertrophy
Hyperresonant	Air-Trapping
Flattened Diaphragm	Air-Trapping
Hyperlucency on CXR	Air-Trapping
Weight Loss	Accessory Muscle hypertrophy, ↑ work of breathing
Prolonged Expiration	Overcoming ↑ Airway Resistance
Pursed Lips	Overcoming ↑ Airway Resistance
Hypoxia	Interstitial Inflammation, Bronchiolar Mucous
Edema	Hypoxia → Pulmonary HTN → R heart failure
RVH	Hypoxia → Pulmonary HTN → R heart failure
RAD	R Heart Failure OR Rotated Silhouette
Cyanosis and Clubbing	Hypoxia
Erythrocytosis	Hypoxia
Hypercapnia	Chronic CO2 retention
Pulmonary Function Tests	Irreversible Bronchoconstriction and inflammation separates wheezing of COPD from wheezing of Asthma. Asthma can be reversed with bronchodilators. Not COPD

Treatment

- Treatment of ***stable, chronic COPD*** is based on an escalation of severity. Many medications can be swapped for each other and this process is much more convoluted (aka personalized) on a patient by-patient basis. Learn the ***mnemonic COPDER and memorize the escalation of therapy we suggest here (knowing that it's more complicated than this).***
- **Short Acting Bronchodilators** (ipratropium, albuterol) are used for acute symptoms relief.
- **Long acting muscarinic antagonists** (tiotropium) is added for initial maintenance therapy.
- **Long acting beta agonists** (formoterol, salmeterol) are added for further maintenance.
- **Inhaled Corticosteroids** (budesonide, another one) are added to reduce readmissions.
- Newer medications such as the **PDE4-Inhibitors** (roflumilast) are a last ditch effort to avoid oral steroids.
- **Oral steroids** are used in refractory disease.

- Notice that in Asthma ICS are added before LABA, but in COPD LABA is before ICS.
- Leukotriene antagonists are used in Asthma, but not in COPD.
- **Corticosteroids** are given in the form of **inhaled corticosteroids** and **oral steroids**. Oral steroids are often reserved for acute exacerbations of COPD and should be avoided in chronic management given the risk of hyperglycemia, hypertension, andosteopenia.
- **Oxygen:** To give or not to give - that is the question. Due to the risk of **eliminating hypoxic drive** (chronic hypercapnia results in respiratory drive driven solely by low levels O2 rather than high levels of CO2) there are strict criteria for starting home oxygen. If the **pO2 < 55** on ABG or **SpO2 < 88%** on a pulse Ox at rest, activity, or exercise, then **chronic home O2** is indicated with a goal of titrating **SpO2 > 88-92%.**
- **Prevention** comes down to **smoking cessation** and **vaccinations**. Patients required the **annual flu vaccine** and the **pneumococcal vaccine**, once before 65 and once after 65. Smoking cessation, in addition to home O2, is the only intervention that will prolong life. However, because there's a lag time between **smoking cessation** and ↓ **inflammation** the patient may initially get worse.
- **Dilators** include any of those listed above: LAMA, LABA, SABA.
- **Experimental** therapy is beyond the level of this course.
- Rehab involves improving exertional capacity but doesn't improve mortality.

Treatment Goals and Methods

C	Corticosteroids	Inhaled maintenance, IV exacerbation, Ø change in mortality unless infection
O	Oxygen	When PaO2 <55 or SpO2 <88% titrating to PaO2 55-60 SpO2 >90%
P	Prevention	Vaccines: Pneumovax (q5y) and Flu (q1y) Smoking cessation ↓ Mortality
D	Dilators	Anticholinergics > Beta-Agonists Rescues à Nebs à Continuous (inpt only)
E	Experimental	Out of our scope
R	Rehabilitation	↑ Exercise tolerance, ↓ Dyspnea and fatigue Ø Change in Mortality

Exacerbation

- When a patient has a **drop in SpO2** or ↑ **in productive cough** the patient may be presenting with acute exacerbation.
- The goal is first to help them breathe, cover a potential infection, then figure out **what caused the exacerbation.** ***The first line therapy*** is, of course, **Oxygen** while a diagnosis is made.
- ***In a patient with acute dyspnea*** the worry of decreasing hypoxic drive is far overshadowed by the patient's need for oxygen. Then, **nebulized therapy** is crucial. **Ipratropium > Albuterol** (for the

test), but the two are usually given together in practice. **IV Steroids** (methylprednisolone 125mg) or PO Steroids can follow if there's no **improvement** with the nebulizers. No **taper is required for COPD. Antibiotics** are **indicated** if there's purulent sputum or sputum production is increased. Use anything that will cover for the typical bugs (**amoxicillin, trimethoprim-sulfa, azithromycin, doxycycline, on a rotating schedule**).

- If there's no improvement **admission to the ICU with mechanical ventilation may** be required.

Interventions in COPD

Agent	*Dose*	*Comments*
Ipratropium	0.5mg NEB q4	First Line
Albuterol	2.5 mg NEB q4	Firt Line
Corticosteroids	Methylprednisone 125mg IV Prednisone 40mg PO	Exacerbation
Oxygen	Titrate to SpO_2 88-92% or PaO_2 55-60	Home and In patient
Intubation and Ventilation		Last Resort

INTERSTITIAL LUNG DISEASE

Introduction

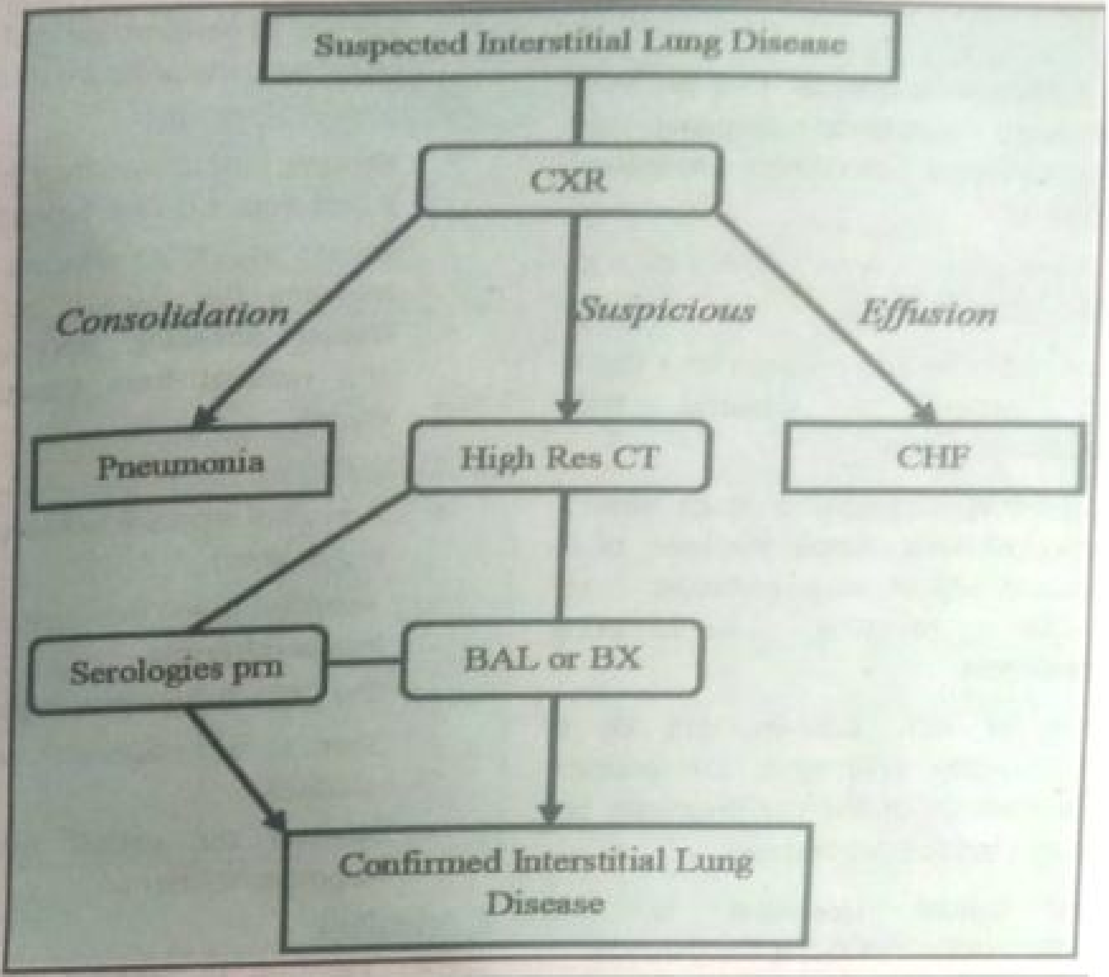
- Interstitial lung diseases (of which there are 200) are all characterized by their restrictive lung patterns demonstrated by the pulmonary function tests. **↓FEV1, ↓FVC, a normal FEV1/FVC, ↓LV**, and a **↓DLCO**. Additionally, most are **amendable to treatment**. Because treatment is futile the quest for diagnosis ***beyond "restrictive lung disease"*** is generally not done. The goal is to exclude those diseases that we can do something about or where toxic exposure can be avoided to ↓ exacerbations of the condition.
- Dividing the disease into ***categories (Known Causes, Collagen Vascular, and Granulomatous)*** is an academic exercise that helps keep the more common diagnoses straight; the true diagnosis list is far more complex. As to what's actually done with patients - the goals are to **remove patients from toxic exposure, administer O2** to prevent hypoxia, and **maintain exercise tolerance**.
- In terms of differentials, ILD are **chronic diseases** with an insidious **onset of signs** and symptoms (**dyspnea and dry cough**) and chest x-ray findings (**patchy infiltrates**).
- This has two consequences:

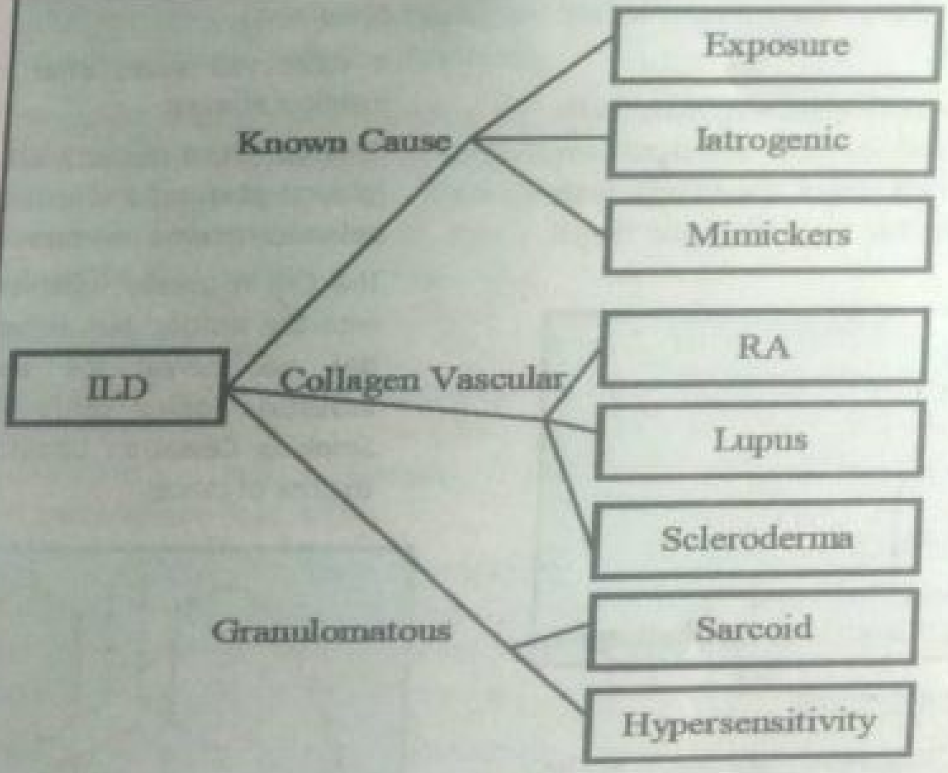
1) The patient may not **recall or consider** a potential exposure **because it may be** remote

2) rapid changes exclude **ILD and generate** a differential for a restrictive **pattern with** acute onset. ILDs should **occur in older patients with a history of toxic exposure**.

1. Granulomatous Diseases

- Really this means "it's not always sarcoid."
- Without extrapulmonary **manifestations**, be careful about presuming a disease that sounds an awful like sarcoid is sarcoid – even when a biopsy shows non-caseating granulomas.


Suspected Interstitial Lung Disease
CXR
Consolidation
Suspicious
Effusion
Pneumonia
High Res CT
CHF
Serologies prn
BAL or BX
Confirmed Interstitial Lung Disease

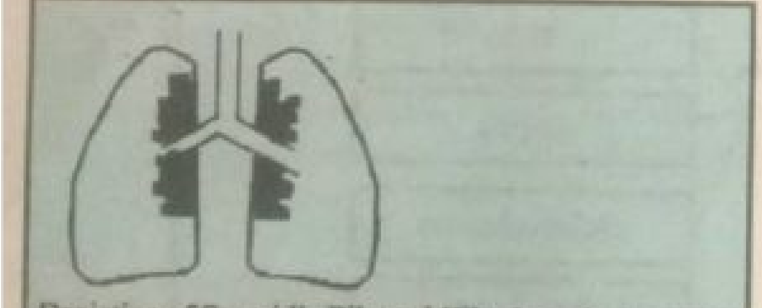

Exposure
Iatrogenic
Known Cause
Mimickers
RA
ILD
Collagen Vascular
Lupus
Scleroderma
Sarcoid
Granulomatous
Hypersensitivity

1st Test = CXR
then = High Res CT
Best = Biopsy

PFTs = ↓Everything
Serology
Bal

I. Sarcoid

- An **autoimmune disorder** that has both pulmonary (**exertional dyspnea**) and extrapulmonary (**erythema nodosum**) symptoms.
- A low-grade fever indicates an inflammatory process.
- It's a restrictive lung disease with a classic **CXR** pattern = **Bilateral Hilar Lymphadenopathy**.
- A definitive diagnosis is made with a **biopsy of lung tissue** (biopsies of E nodosum will show E nodosum - not sarcoid) revealing **noncaseating granulomas**.
- Levels of **ACE**, **Calcium**, and **Vit D** (noncaseating granulomas can produce their own Vit D) are non-diagnostic but can be used to track therapy.
- The ***typical treatment*** is with **Methotrexate** and **Cyclophosphamide**.
- Therapy may change for extrapulmonary manifestations.
- **Uveitis** can lead to blindness, while **Bells Palsy** and **E. nodosum** can add significant morbidity. Treat these conditions with **steroids** (especially the uveitis) and they'll improve.



Depiction of Sarcoid's Bilateral Hilar Lymphadenopathy

I. Hypersensitivity Pneumonitis

- Also an "exposure" disease, it too produces **non-caseating granulomas** secondary to exposure to **pigeon feathers**, **organic dust**, or **actinomyces**. It's generally self-limiting. Look for birds and farms in the exposure history. This is included to demonstrate that not all non-caseating granulomas are sarcoid.

2. Occupational Exposures

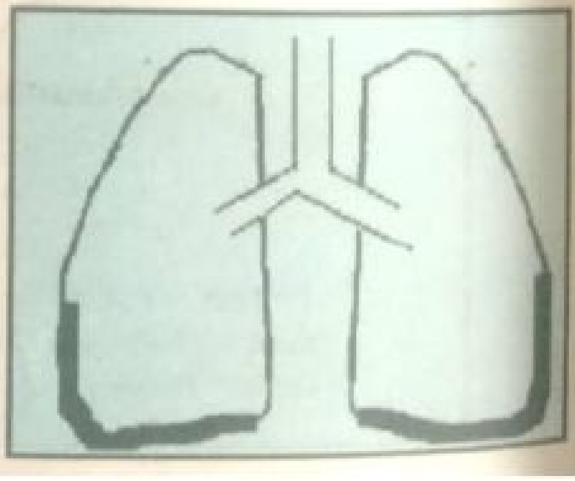
- Fibrosing lung disease from toxic exposure is both **dose** and **time** dependent.
- There's usually no effective therapy for reversing the disease, but **associated disease screening**, **smoking cessation**, and **removal from exposure** become crucial.

I. Pneumoconiosis

- A result of exposure to **heavy metal** (gold, nickel, silver).
- Patients have the typical course of **insidious hypoxia**.
- The CXR will show **ground-glass opacities**.
- There's no treatment or associated diseases.
- Remove the patient from whatever exposure he/she had.

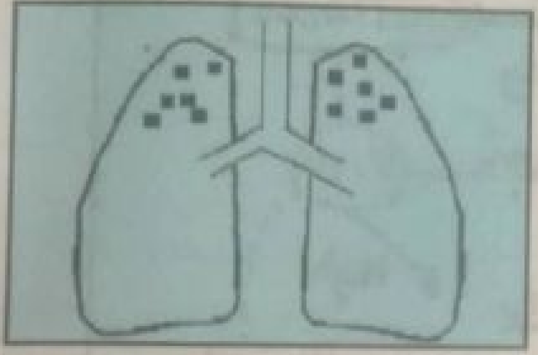
II. Asbestosis

- Exposure to **asbestos** (shipping yards, demolition).
- It takes **>30 years** after **exposure** to manifest disease.
- This has both a characteristic CXR pattern (**pleural plaques**) and associated disease (**adenocarcinoma** and **mesothelioma**).
- The CXR is usually sufficiently diagnostic with the history, but either a **Biopsy** or **BAL** will reveal the barbell shaped **asbestos bodies** confirming diagnosis. **Smoking Cessation** significantly reduces the risk of cancer.



III. Silicosis

- Exposure to **rock dust** (quarries, blasting) and **sand blasting**.
- The unique CXR finding is the **upper lobe nodules**.
- This has a differential of TB, but also a higher association with TB than the others.
- There's tx but patients should be **screened annually for TB**.



Coal Miner's Lung

- Exposure is to **coal**.
- The only thing pertinent to this disease is the association with **Caplan Syndrome**.
- A patient with a restrictive lung pattern and a **bilateral symmetrical Arthralgia** should be worked up for **rheumatoid arthritis** with a Rheumatoid Factor or **Anti-CCP Ab**.

3. Known Causes

i. **Iatrogenic** causes include **Bleomycin** and **amiodarone** that has a pattern similar to Interstitial Lung Fibrosis and Hypersensitivity Reactions

ii. **CHF** causes **Effusions**, replacing parenchyma with fluid, thereby ↓the functional space. Typically **acute** and **reversible**. This may initially mimic ILD.

iii. **Infxn** **Bacteria** replace parenchyma. Typically **Acute** and **Reversible.** This may initially mimic ILD.

iv. **Cancer** replaces the parenchyma and contracts it down. While **chronic and irreversible,** it too may mimic ILD.

LUNG CANCER

Introduction

- Lung cancer is a common malignancy and cancer killer.
- It's very tightly linked to smoking.
- While exposure to radiation, heavy metals, and some other workplace scenarios (like Asbestosis) do contribute to lung cancer, you should align "Smoking" and "Lung Cancer" as essentially synonymous (especially in regards to the test).

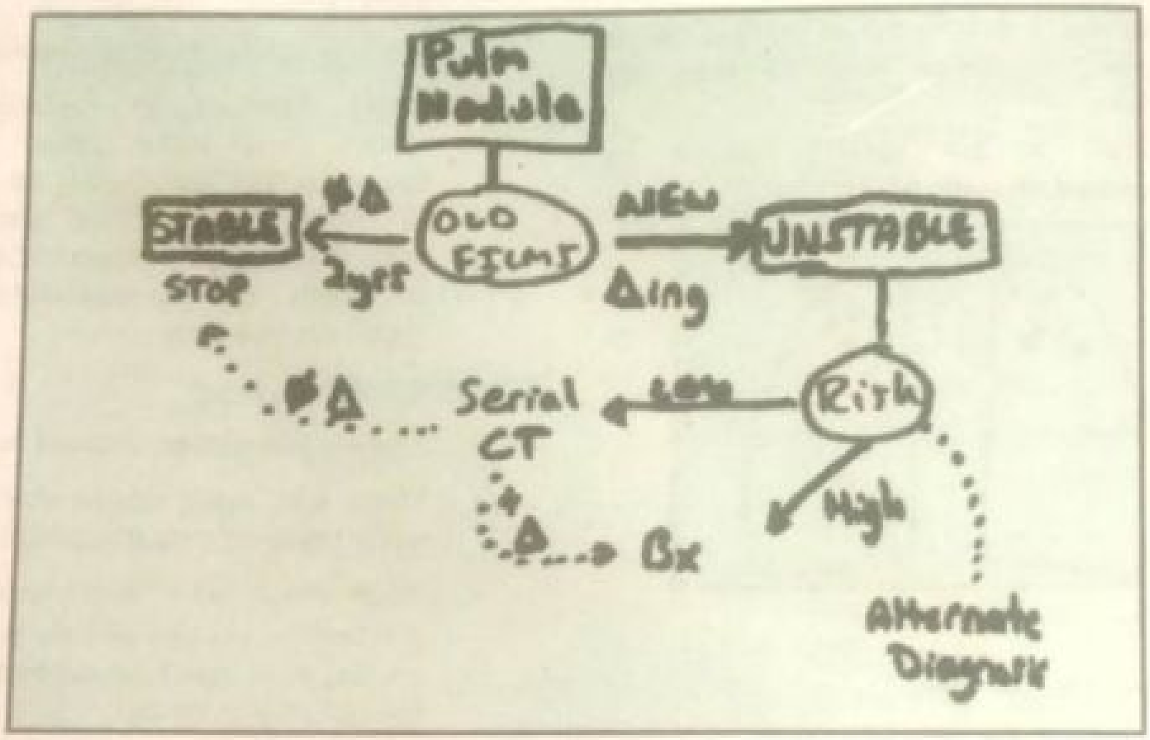
Screening and Prevention

- **Primary prevention** is about **not smoking.**
- Those who don't smoke shouldn't start, while those who do should quit today.
- Even those who don't smoke should avoid other people who do (second hand smoke) as all smoking exposure increases the risk of lung cancer.
- **Screening** is with an **annual Low Dose CT scan** of the chest.
- The people who get screened are those who have a **30 pack year** history, quit **less than 15 years ago**, and are between **55-80** years old.

Pulmonary Nodule

- Regardless of whether a **pulmonary** nodule was found because of a **screening** CT scan or from imaging of the chest for some other reason, the investigation process is the same.
- Step one is to **compare old films**. If there's been **no change** in **2 years**, the nodule is said to be stable; no further investigation or follow-up is required.
- If the nodule has changed, it's said to be **unstable**; the decision becomes whether or not this can be followed with **serial CT scans** (for two years until it becomes stable) or needs to be **biopsied right now.** The things that make the risk increase or

decrease are listed below. We've come up with the "S"s as a means of helping you remember which cancers are caused by smoking and to remind you that the analysis of a nodule is made using **Size**, **Surface features**, **Smoking history**, and the patients **Age (Self)**.



Diagnosing with Tissue, Different Approaches

Not Cancer		*Is Cancer*
<8 mm	Size	> 2 cm
Smooth, Calcified	Surface	speculated
No smoking <45	Smoking	>30 yr
	Self (Age)	hx > 70

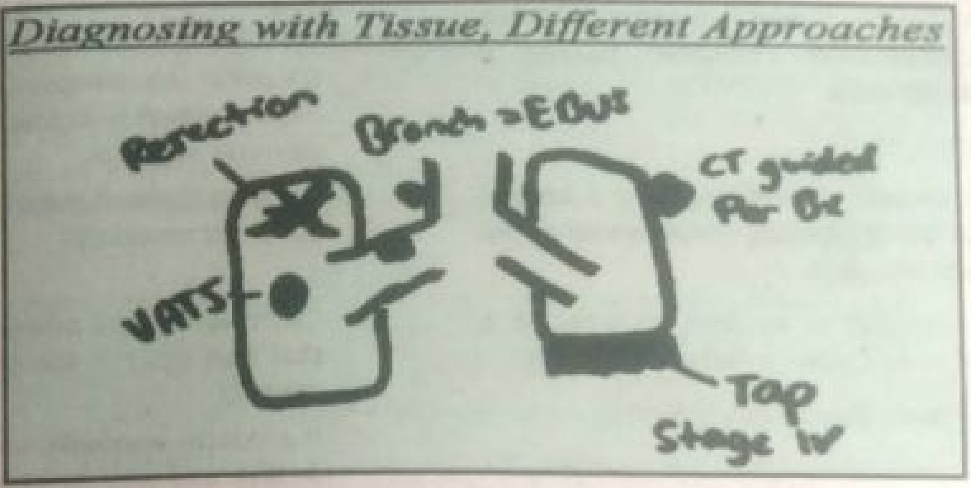
Making a Diagnosis of Lung Cancer

- Lung cancer can occur in different places in the lung and often spreads through lymph nodes prior to metastasizing.
- The major rule of lung cancer is to avoid poking the lung if possible; make the diagnosis some other way.
- Ideally, that means stage the cancer and make the diagnosis by choosing a site that is extra-pulmonary.
- But for intrapulmonary lesions without evidence of spread, there are still a number of ways to get a piece of tissue.
- The **Bronchoscopy** (now upgraded to include an ultrasound probe called **EBUS**) is used to biopsy proximal lesions.
- Rigid bronchoscopy alone allows us to sample lesions that are intraluminal in large airways, while EBUS allows for more accurate sampling of the lymph nodes or masses on the outside of the lumen (in the chest / lung).
- **Percutaneous CT guided biopsy** is chosen when the lesion is peripheral.
- **Video Assisted Thoracoscopic Surgery** (the laparoscopy of the chest) can be used

to sample lesions not assessable by EBUS or Percutaneous biopsy.

- Still other methods exist.

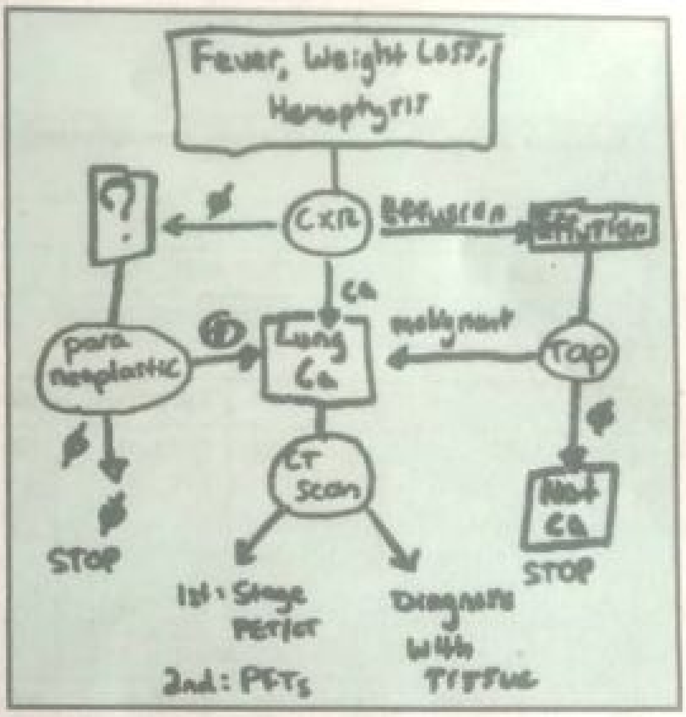
- **Thoracentesis** revealing malignant cells is Stage IV, metastatic disease. And lesions that are very clearly malignant can be diagnosed with **resection**.


Diagnosing with Tissue, Different Approaches

Resection
Bronch > EBUS
CT guided Per Bx
VATS
Tap
Stage IV

Lung Cancer Presentation

- The classic symptoms of an advanced lung cancer include **fever, hemoptysis,** and **weight loss**.
- These are constitutional symptoms seen in Lymphoma and in TB.
- ***But if the person is old*** and has a personal history of smoking, you're being guided towards Lung Cancer.
- Often the workup begins with a Chest x-ray, done not because it's lung cancer (Chest x-ray is poorly sensitive for Lung Cancer), but as an inexpensive and accessible means of looking at the chest.
- If lung cancer is suspected, go straight to CT scan.
- If that chest x-ray is **unrevealing,** but there **are paraneoplastic syndromes** get a CT.
- If the x-ray reveals an effusion, perform **thoracentesis.**
- If the CT scan shows a malignancy, refer to the diagnostic approaches listed above.
- Staging is done with **PET-CT.** before a treatment plan is made, **pulmonary function tests** are required to assess if the patient can tolerate surgery.
- Then, ultimately chemo, radiation, and surgery are chosen based on the stage.


Fever, Weight Loss, Hemoptysis
?
ø
CXR
Between
Effusion
Ca
para neoplastic
⊕
Lung Ca
malignant
Tap
ø
ø
ø
CT Scan
STOP
Not Ca
STOP
1st: Stage PET/CT
2nd: PFTs
Diagnose with Tissue

Squamous Cell Carcinoma

- Caused by **smoking,** the lesion is typically **central**.
- Classic warning signs (**hemoptysis** and **weight loss without fever**) are the tipoff.

- A CXR may show a large lesion or repeated PNA (caused by obstructing lesion).
- **EBUS with Biopsy** gets the diagnosis.
- The cancer may produce **PTH-rp** (parathyroid-like hormone) causing a **hypercalcemia.**

Small Cell Carcinoma

- Also caused by **smoking.** It's a **central** lesion that's **typically metastasized** at the time of diagnosis.
- It's too small to be seen on X-ray so it requires a **CT scan** to make the diagnosis.
- **EBUS with Biopsy** will confirm it.
- The tumor should NOT be resected; it's **exquisitely sensitive to chemo.** Because it's a neuroendocrine tumor it can produce **ADH** (SIADH) or **ACTH** (Cushing's).
- It doesn't get large enough to cause obstructive pneumonias or hemoptysis.

Adenocarcinoma

- This is the lung cancer that people get when they **don't smoke.**
- It typically occurs in the **periphery** of the lung and is stuck to the **pleura** causing it **to pucker.**
- It's either spontaneous or secondary to a remote **asbestos exposure** or other non-cigarette exposure.
- Smoking makes it more likely, and worse, but is not necessary.

Carcinoid

- Carcinoid is a rare neuroendocrine tumor that may occur in the small intestine or the lung.
- It produces **serotonin,** which degrades to **5-HIAA** and gets secreted into the urine (how it's diagnosed). Because the serotonin originates in the lung it will cause a **left-sided valve fibrosis** along with the flushing, wheezing, and diarrhea typical of the intestinal carcinoid.
- Since the serotonin is degraded by the liver, the right side of the heart is spared.

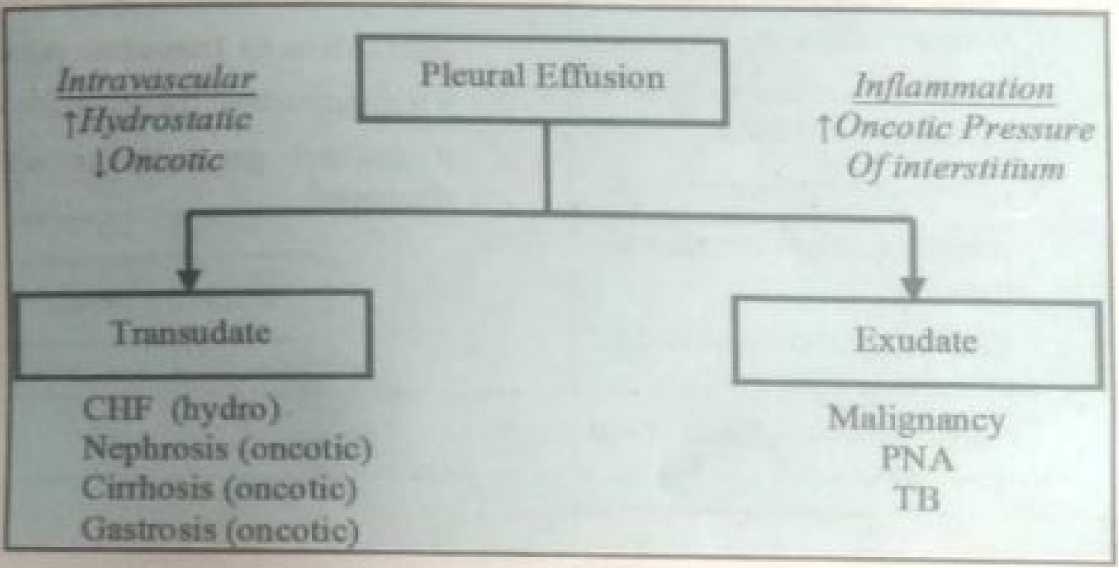
Surgery Alone	*Surgery and Adjuvant Chemo*	*Chemo Radiation WITHOUT surgery*
In	Ib> 4 cm Mass	
In, <4cm mass	II (N0 or N1 nodes)	IV (N2, N3 nodes)
	III (N0 or N1 nodes)	IV (mets)
		IV (Pleural effusion)

Cancer	*Path*	*Location*	*Histology*	*Paraneoplastic*	*Dx*	*Ix*
Small Cell	Smoking	Sentral	Neuroendocrine granules on EM	ADH - SIADH ACTH – Cushing's	Bronch, EBUS	Chemo + Rad (no matter the stage)
Squamous Cell	Smoking	Sentral	Intracellular Bridges, Keratin Pearls	PTH-rp	Bronch, EBUS	Surgery
Adenocarcinoma	Asbestos	Peripheral	Mucin Glads	-	Perc CT	Surgery
Carcinoid	Smoking	Anywhere	Salt and Pepper	Serotonin Syndrome	U 5-HIAA	Surgery

PLEURAL EFFUSION

Pathogenesis

- There are two types of effusions: transudates and exudates.
- A **transudate** is a lot of **fluid** and not much else.
- It's caused by **intravascular pathology;** either an **↑Hydrostatic Pressure** (CHF) or **↓Oncotic Pressure** (Nephrotic syndrome or cirrhosis) from within the blood vessels.
- These are usually distributed evenly across the lungs and are thus **bilateral**.
- An **exudate** is a lot of **stuff** in the parenchyma drawing the fluid out. It's caused by **inflammation** – the capillaries become leaky, and protein and fluid leak out. There's "Stuff" in the space. Since this doesn't necessarily distribute evenly it may be **unilateral**.



Diagnosis

- Pleural effusion is on the differential for shortness of breath or pleuritic chest pain.
- However, the diagnosis does not become apparent until the **Chest X-ray.**
- Once **blunting of the costovertebral angles** (which requires at least 250cc) is seen the diagnosis is made.
- If more than that is present the **air-fluid level** (the meniscus) rises.
- After the chest X-ray perform a **recumbent X-ray** to assess if the fluid is **free moving** (not loculated) and in sufficient quantity (**>1cm** from chest wall to fluid level) to do a **thoracentesis**.
- A loculated effusion can't be safely tapped; it needs surgical intervention.
- With thoracentesis the **Light's Criteria** (comparing the **Serum Protein** and **Serum LDH** to the **Pleural protein** and the **Pleural LDH**) can be performed.
- It shows the exudates vs transudates (see the table to the right). The next need is to get a complete characteristic of the pleural fluid for definitive diagnosis (**WBC**, **RBC**, **pH**, and **Glucose**).
- **CT scan** or **bedside ultrasound** can also assess for loculation. The CT may also give insight into the cause of the effusion. You really can't be asked to choose between them on a test. In life the ultrasound is the most reliable because you see it + do the tap under imaging guidance.
- If **CHF, diurese only** unless it fails to resolve with diuresis.

Upright Chest X-ray

<250cc	Not visible
250cc	Blunting of the costovertebral angle
>250cc	Meniscus line rises, air-fluid level

Recumbent Chest X-ray

Free fluid vs loculated (Layers out or doesn't) Volume required for thoracentesis (>1 cm)

Thoracentesis Findings

Transudate	LDH < 2/3 Upper Limit of Normal (~200) and Total Proteineffusion / Total Proteinserum<0.5 and LDHeffusion / LDHserum < 0.6
Exudate	LDH > 2/3 Upper Limit Normal (~200) or LDHeffusion / LDHserum > 0.6 or Total Proteineffusion / Total Proteinserum>0.5

CT Scan

If underlying conditions require for evaluation or diagnosis

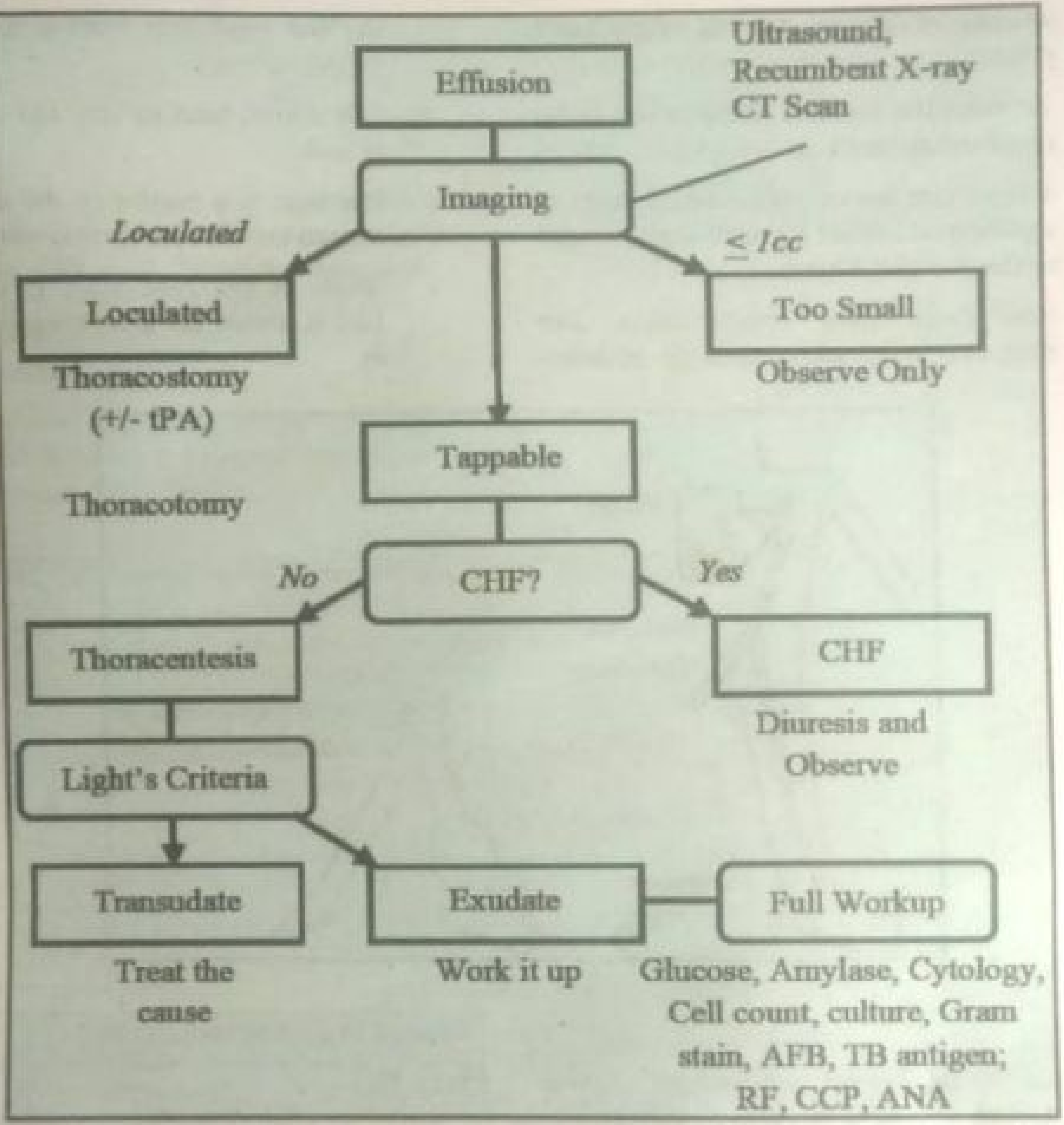
Treatment

- If there's a loculated effusion a **thoracostomy** (chest tube) is required.
- Parapneumonic effusions that are loculated may form a rind, called **empyema**.
- This requires **thoracotomy** (surgery) with decortication.
- Repeat effusions may be treated with **pleurodesis** – a chemical or surgical elimination of the pleural space.
- If a pathology is identified on the thoracentesis, treat the underlying condition.
- If the condition is already known, no tap need be done (for example, **CHF getting diuresis only**).

Overview

1) Find an effusion on CXR à Determine **Tappability**
2) a. If loculated, **thoracotomy** … failure… **thoracotomy**

   b. If not loculated >1cc **Tap**, if <1cc **Observe**
3) If they have CHF diurese and monitor - do **NOT tap**
4) Light Criteria for **Transudate vs Exudate**
5) If transudate treat the underlying disease
6) If exudates get complete workup, tx as diagnosed


Effusion
Ultrasound,
Recumbent X-ray
CT Scan
Imaging
Loculated
≤ 1cc
Loculated
Thoracostomy
(+/- tPA)
Thoracotomy
Too Small
Observe Only
Tappable
No
CHF?
Yes
Thoracentesis
CHF
Diuresis and
Observe
Light's Criteria
Transudate
Treat the
cause
Exudate
Work it up
Full Workup
Glucose, Amylase, Cytology,
Cell count, culture, Gram
stain, AFB, TB antigen;
RF, CCP, ANA

PULMONARY EMBOLISM

Introduction

- Pulmonary embolism should be considered one continuous disease with a deep venous thrombosis.
- The etiology of DVT / PE is **Virchow's Triad:**

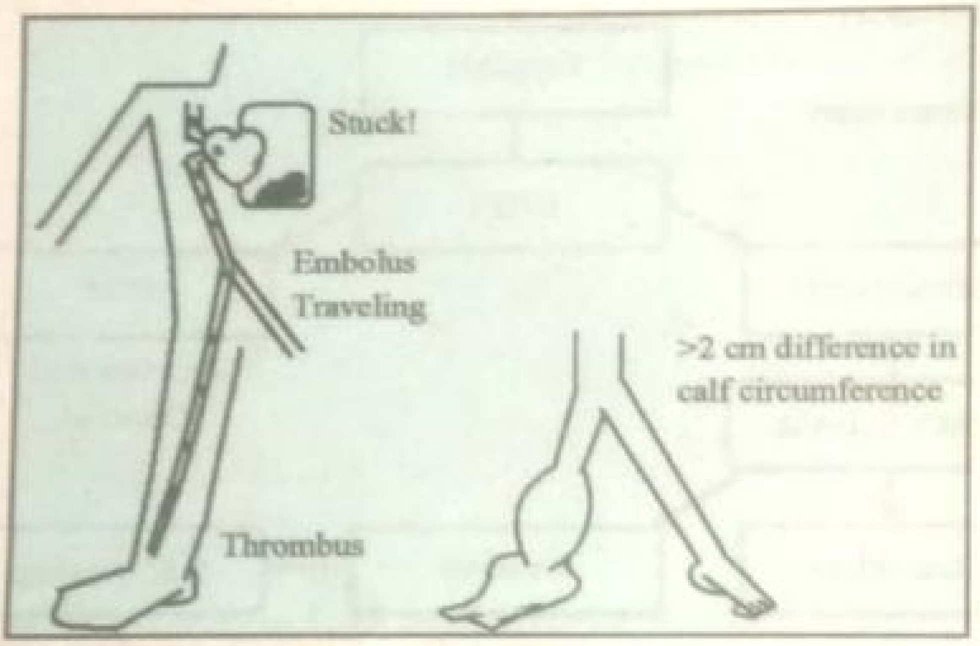
  1) **Venous Stasis,**

  2) **Hypercoagulable State,**

  3) **Endothelial Damage.**
- Risk goes up with the classic risk factors (bed rest and surgery), hypercoagulable disorders (cancer, OCPs, and genetics), and HTN/Dissection/IV sites.
- The **thrombus forms** in the **deep veins;** it's typically in the **popliteal** or **femoral** veins. Since there are **valves** in the deep veins, should a piece of a clot should break free (the **embolus**) it can travel up the IVC and into the lungs. It gets stuck in a small vessel of the lung.
- This has two consequences. 1) Because good blood is unable to get to the alveoli, there's a **limitation of gas exchange**. 2) Because there's less piping to pump blood through there's an increase in **pulmonary**

vascular resistance, creating a **right heart strain**.

- Yet even the smallest embolus can cause profound dyspnea.
- A small clot doesn't cause heart strain or significantly impact gas exchange (relative to the size of the lung).
- How these small emboli cause such profound dyspnea is through **platelet-derived mediators** leading to lung-wide inflammation.
- This allows fluid to leak out around the alveoli.
- The fluid is a barrier to the diffusion of oxygen but NOT carbon dioxide.
- Thus, as the respiratory rate increases **CO2 is blown off** while **Oxygen can't get in**.



Presentation

- The classic patient will present with a **shortness of breath**, **tachypnea**, **tachycardia**, a **pleuritic chest pain**, and a **Clear Chest X-ray**.
- The difficulty with PE is that there's no clinical finding that screams "PE here," so the goal is to identify risk factors and rule out other diseases.
- Stop checking for Homans sign – it's useless.
- Instead, look for **one leg that has a larger circumference than the other**, which is suggestive of a DVT.
- Use the **Well's Criteria** to decide what type of test to do and how to treat it.

Wells Criteria – Building the Wells Score

PE most likely diagnosis, s/s DVT	3 each
HR > 100	1.5
Immobilization	1.5
Surgery w/i 4 weeks	1.5
Hemoptysis	1
Malignancy	1
h/o DVT or PE	1.5

Wells Score – for V/Q Scan Interpretation

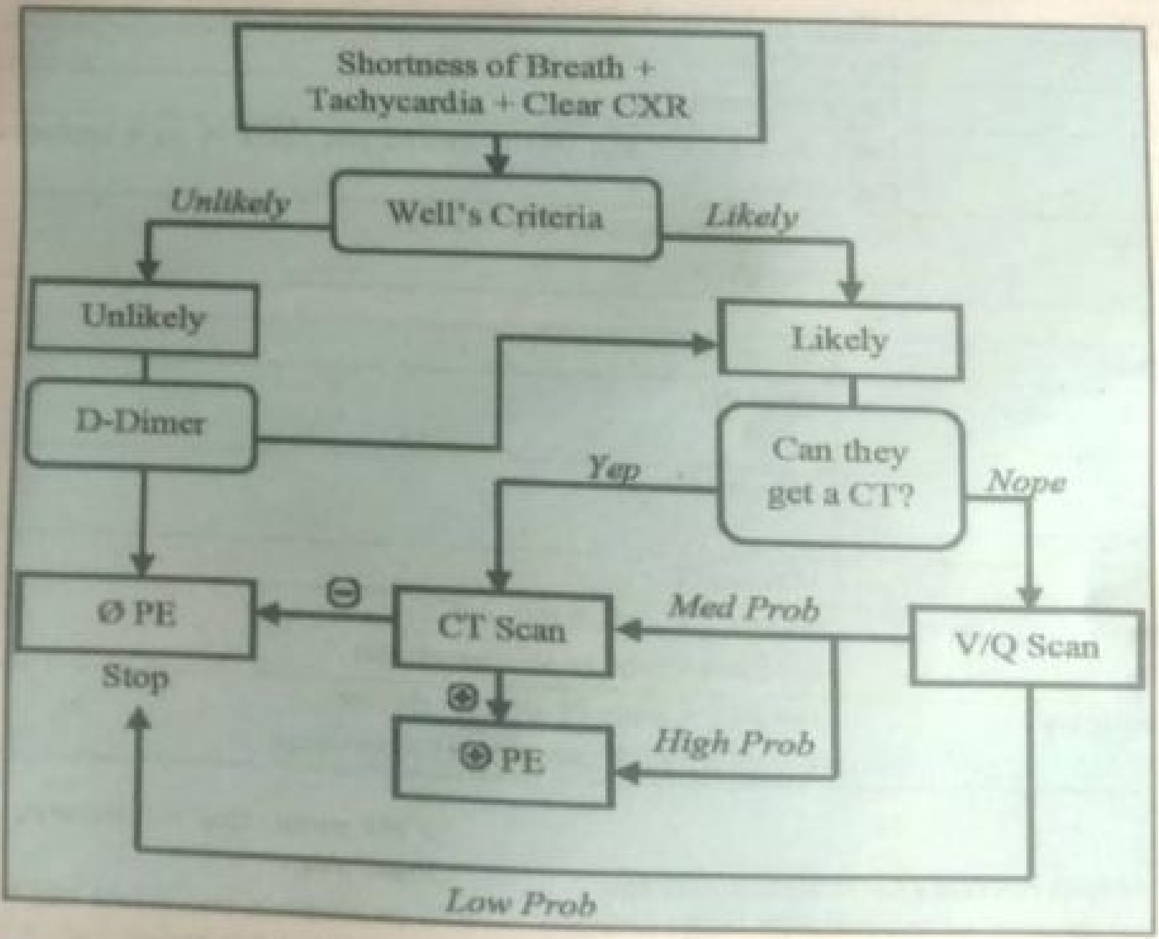
Score <2	Score 2-6	Score > 6
Small Probability	Moderate Probability	High Probability

Modified Wells – do I do a CT Scan?

Score ≤4	Score >4
Don't do it	Do it

Diagnosis

- During the workup of SOB the typical tests of **CXR**, **EKG**, and **ABG** may show soft signs of PE.
- The CXR is normal - the EKGS show **S1Q3T3** indicative of Right Heart strain - and the ABG may show a **hypoxemic respiratory alkalosis** (the increased respiratory rate because of hypoxia drives venting of CO_2).
- The absence of these mean nothing, however. A **D-Dimer** is useful only if the pre-test suspicion is low and you're **ruling out PE** with a **normal D-Dimer**. Any inflammation can raise the D-Dimer; a positive D-Dimer does not mean PE.
- **CT Angiogram** is the best test. An angiogram-with-a-wire is basically not used anymore. Both require contrast.
- A **V/Q scan** can be used if there's CKD or AKI, but only if there are **clear lungs**.
- **If all else fails**, since a DVT is treated the same as PE, an **ultrasound** can be used to diagnose DVT as a proxy if no test is available for PE.


Shortness of Breath + Tachycardia + Clear CXR
Well's Criteria
Unlikely
Likely
Unlikely
Likely
D-Dimer
Can they get a CT?
Yep
Nope
⊖
Ø PE
Stop
CT Scan
Med Prob
V/Q Scan
⊕
⊕ PE
High Prob
Low Prob

Treatment

- Treatment is really based on the severity of the disease.
- If there's a **massive embolism** that has compromised cardiac function (hypotension) it's imperative to jump right to emergent intra-arterial **tPA**.
- In **most cases** there are ***two treatment goals***. One is to shut off those **platelet mediators** using **heparin**. Heparin is the mainstay of therapy; start it even if a PE is suspected. ***The second goal*** is to **prevent recurrence** with an anti-coagulator like **warfarin**. To put a patient on heparin they need a **heparin to warfarin bridge**. The

target INR is 2-3; give heparin to help the patient right now and to prevent the pro-coaguable effects of early warfarin.

- **Novel oral anticoagulants** such as rivaroxaban or apixiban are acceptable alternatives to warfarin. They can't be reversed and are twice a day, but also don't require monitoring.
- The only time an **IVC Filter** is the right answer is when there's a DVT, the next PE will kill them, AND there's a **contraindication to anticoagulation**.
- **Thrombectomy** is used to manage chronic thromboembolic pulmonary hypertension. It's not used in the acute management of disease.

Pulmonary Embolism

***Path:** Virchow's Triad*

***Pt:** Shortness of Breath, Tachycardia, Clear CXR*

***Dx:** D-Dimer, CT Scan, V/Q Scan*

***Tx:** Heparin to Coumadin*

Test	When
D-Dinner	Low probability, rule out DVT/PE
V/Q	Elevated creatinine AND clear lungs
CT scan	Preferred test for PE
U/S Legs	Can't do a CT or VQ; DVT is treated just like a PE so it approximates diagnosis
Angiogram	Not for acute management. CT scan is good enough

Treatment	When
LMWH to Warfarin bridge	Most PEs
Heparin to Warfarin bridge	Submassive PE
tPA	Massive PE
IVC Filter	~Never, only when DVT and contraindication to Anticoagulation
Thrombectomy	Not during acute PE, only for chronic thromboembolic pulmonary hypertension

Monitoring

- Warfarin can cause hypercoagulability and thus requires a heparin bridge in the first few days.
- Likewise, INR must be maintained between 2-3 to avoid bleeding (if it gets too high) and clotting (if it gets too low).
- While in the hospital, **heparin** can induce a **heparin induced thrombocytopenia** (HIT). This usually occurs within ***7 days on first exposure and 3 days on repeat.*** Draw a **HIT panel**, stop the Heparin, and give **Argatroban.**
- If ***on warfarin,*** you should also know how to manage what happens when the INR is not at goal.
- If the warfarin is **sub-therapeutic** they must be **put back on heparin and bridged** to therapeutic.
- A bridge must be a **minimum of 5 days** and as long as it takes to get therapeutic.

- Low molecular weight heparin (fondaparinux, enoxaparin) are just as good as a heparin infusion, and are far more convenient for the patients.
- If the INR is **supratherapeutic**, there are a few options.

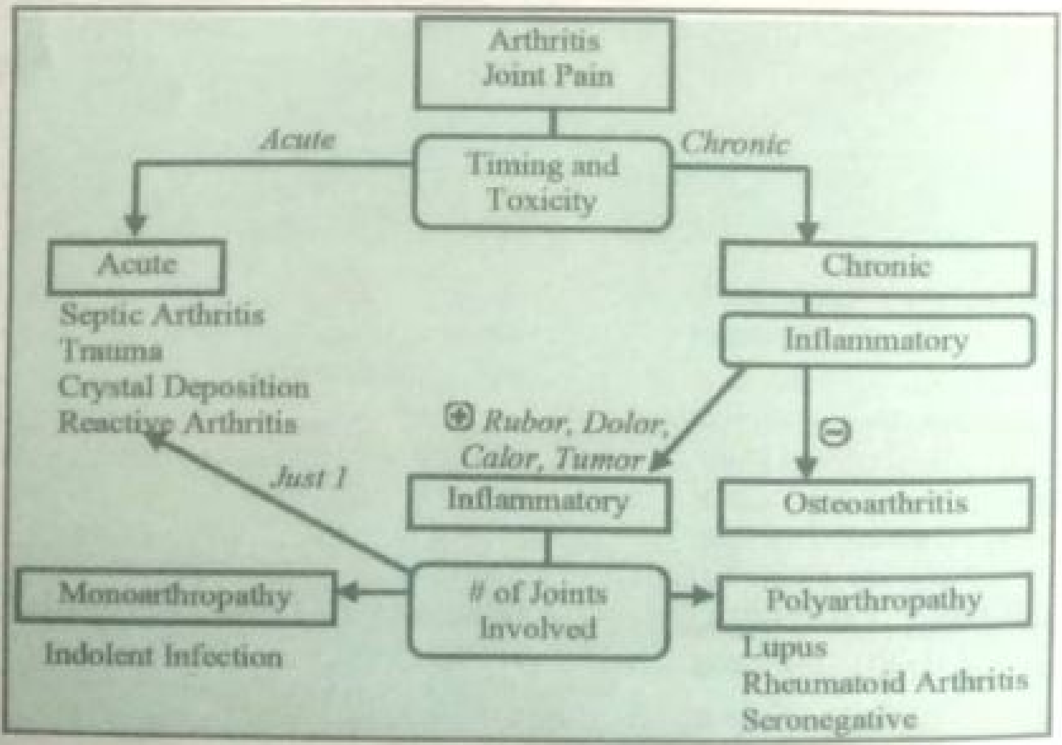
INR	Bleeding	Action
<5	No	Hold a dose
5-9	No	Hold dose, Vit K
>9	No	Hold dose, Vit K, lower dose
Any	Bleeding	FFP, Vit K

RHEUMATOLOGY

APPROACH TO JOINT PAIN

Differential Diagnosis

- Rheumatology is essentially the diagnosis and management of joint pain.
- It has quite an extensive differential as it could be the primary complaint or the symptomatology that links all disease.
- Unfortunately, many of these diseases have a **list of associated symptoms** that have be memorized in order to ascertain the correct diagnosis.
- However, there are some classifications that can help reduce the potential list of diagnoses.
- The **number of joints**, **pattern**, and **symmetry** of joint pain play a huge role.
- Usually **monoarticular** involvement has to do with a disease of **that joint**, indicating an absence of systemic involvement.
- It's often acute. **Polyarticular** involvement is associated with systemic disease.
- Let's break it down further. In polyarticular disease **absence of symmetry** means it's likely **degenerative** as it reflects the asymmetry of use.
- If there's **symmetry** it indicates autoimmune.
- Finally, even paying attention to **WHICH joint is involved** can be useful (RA spares the DIP for example).
- Besides that, **extrarticular manifestations** are often unique to a given diagnosis, though crossover does exist.
- The important thing is that **no one finding** is sensitive or specific – it's the combination of symptoms that lets the diagnosis comes to light.
- Using this algorithm may be useful, but it's the memorization that excels in rheumatology.


Arthritis
Joint Pain
Acute
Timing and Toxicity
Chronic
Acute
Septic Arthritis
Trauma
Crystal Deposition
Reactive Arthritis
Chronic
Inflammatory
⊕ Rubor, Dolor, Calor, Tumor
⊖
Just 1
Inflammatory
Osteoarthritis
Monoarthropathy
# of Joints Involved
Polyarthropathy
Indolent Infection
Lupus
Rheumatoid Arthritis
Seronegative

Arthrocentesis

- If you see a red, hot, swollen joint, the answer on the test will be **Arthrocentesis**.
- The diagnosis can be made without an arthocentesis (history of gout that has a gouty flare), but your reflex should be to tap the joint.
- In a **normal joint** there should be a bunch of fluid - that's it.
- In **degenerative disease** it's the same; the joint is just degraded (neither normal joint or degenerative joint conditions should have prompted a tap).
- On the other end of the spectrum, a **septic joint** will be full of **pus**: white, opaque, LOTS of cells, LOTS of polys. **50,000** is the number to remember.
- If there are more than 50,000 WBCs it's septic, regardless.
- An **Inflammatory joint** will be somewhere in between; it'll have some cloudy fluid, some cells, and mostly polys.
- The presence of **staph** tells you septic.
- If septic and no organism, be cautious of **gonorrhea** and get a NAAT or chocolate agar culture.
- The presence of **crystals** clues us in on crystal disease.
- Inflammatory joint without organisms or crystals means "it's a rheumatologic disorder" and little else.

Single Joint	**vs**	**Multiple Joints**
Septic Crystals	vs	Osteoarthritis, Lupus, Rheumatoid Scleroderma, Myositis, Seronegatives
Acute	vs	***Chronic***
Septic, Trauma, Crystal, Reactive	vs	Osteo, Lupus, Rheumatoid, Scleroderma, Myositis, Seronegatives
Isolated	vs	***Systemic Manifestations***
Septic Crystal		Seronegative (IBD) Lupus (Face, CNS, Renal, Heart, Lung) Rheumatoid (Nodules, Serositis) Reactive (Oral + Genital Ulcer)
Degenerative	vs	***Inflammatory***
Osteoarthritis	vs	Everything Else

	Normal	*Non Inflammatory*	*Inflammatory*	*Sepsis*
Appearance	Clear	Clear	Yellow, White	Opaque
WBC	<2	<2	>2, <50	>50
Polys	>25%	25%	≥50%	>75%
Gram/Cx	⊖	⊖	⊖	⊕
Dz	None	Osteorathritis	Everything Else	Infection

WBC is "thousands"

Antibodies

- Bottom line: **there isn't one test, but rather a combination of findings** (including serology) that leads to diagnosis

Antibody	*Interpretation*	*Antibody*	*Interpretation*
ANA	Sensitive Lupus	RO+LA	Sjogren's
Histone	Specific Drug-Induced Lupus	CCP	Rheumatoid Arthritis
ds-DNA	Specific Lupus + Renal Involvement	RF	Rheumatoid Arthritis
Smooth Muscle	Autoimmune Hepatitis	Jo	Polymyositis
Mitochondrial	Primary Biliary Cirrhosis		
Centromere	Scleroderma (CREST	Topoisomerase (Scl-70)	Systemic Scleroderma

LUPUS

Introduction

- Lupus is an **autoimmune disease** mitigated by **complement** forming complexes.
- Being autoimmune, it effects **women more than men** and **non-whites more than whites**.
- It is one of the great imitators and can be challenging to make the diagnosis in the early stages.

BAG OF LUPUS
1) Chronic Inflammatory Disorder, Systemic Consequences
2) Joints, CNS, Kidneys, and a Rash Multiarthritic Renal Failure Change in mental status   Malar/Discoid Rash
3) ANA is sensitive, not Specific, 1st test
4) ds-DNA Specific, not sensitive,
5) Possible Drug-induced Lupus with Hydralazine, Procainamide, INH, and α-methyldopa... get an Anti-Histone Ab, stop the drug
6) Treat Arthralgias with NSAIDs Treat Flares with Steroids Treat life-threatening disease with Cyclophosphamide

Presentation (and diagnosis)

- There's **no confirmatory step** or biopsy that seals the diagnosis of lupus.
- Instead, the diagnosis is made with **4 of 11 criteria** being met.
- These 11 criteria can be recalled with either the mnemonic **MD SOAP BRAIN** or via the **hideous monster**.

SOAP BRAIN MD

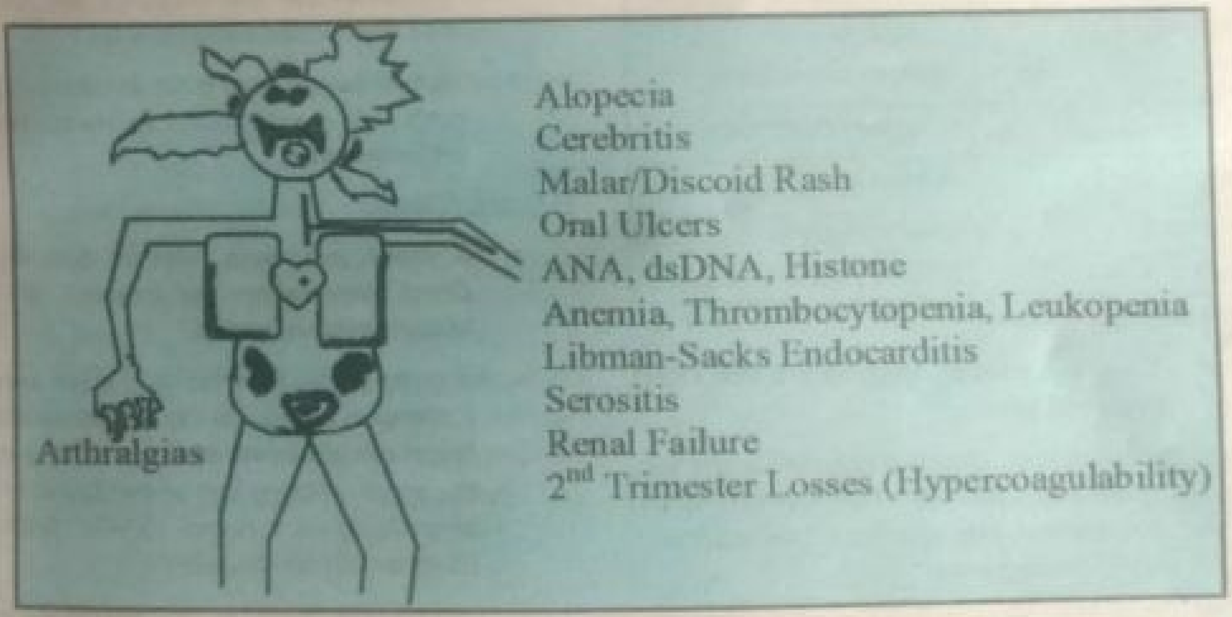
Sesrositis	Blood	Malar Rash
Oral Ulcers	Renal	Discoid Rash
Arthritis	ANA	
Photosensitivity	Immumologic	
	Neurologic	

- The things the patient will care about are going to be the **serositis** (chest pain), **arthritis** (with a predilection for the large joints), and the **face rashes** (malar = butterfly, discoid = disk shaped) or the **skin rashes (photosensitivity)**.
- The things that you'll care about are the **cerebritis** (encephalopathy, psychosis, obtundation), **lupus nephritis** (progressive renal failure), and potentially pulmonary hemorrhage.
- Certain things just jump out on a test.

- **Libman-Sacks-Endocarditis** (LSE) is essentially pathognomonic for Systemic Lupus Erythematosus (SLE).
- The **malar rash** that spares the nasolabial fold and **early trimester losses** are also suspicious for lupus.

Testing (notice this isn't called "diagnosis")

- There is **no confirmatory step**. But certain lab tests can be useful.
- The **CRP** (better than ESR) reflects the disease severity.
- The **ANA** is the gateway antibody – it is highly sensitive but specific for nothing.
- If positive, look for other antibodies: particularly the **anti-histone** (drug-induced lupus), **anti-smith** (lupus), and **ds-DNA** (nephritis).
- If the patient is in an **acute flare** (which may appear septic with fever), obtain **complement levels**.
- If reduced, it's likely to be a flare rather than an infection. Unlike some other autoimmune diseases such as Multiple Sclerosis, lupus doesn't worsen in infection – it may simply be a flare.
- **Anemia** and **thrombocytopenia** can be seen but are neither sensitive nor specific.
- If **lupus nephritis** is suspected a **renal biopsy** is required before treatment.


Alopecia
Cerebritis
Malar/Discoid Rash
Oral Ulcers
ANA, dsDNA, Histone
Anemia, Thrombocytopenia, Leukopenia
Libman-Sacks Endocarditis
Serositis
Renal Failure
2nd Trimester Losses (Hypercoagulability)
Arthralgias

Treatment

- **Hydroxychloroquine for everyone**. Period.
- Everybody who can tolerate the drug gets it.
- Methotrexate can be used if the drug can't be tolerated, but hydroxychloroquine reduces flares and subdues disease.
- **Steroids** are used only in **acute flares**.
- If the disease is severe, or it's a first time diagnosis, use steroids.
- The worse the presentation, the larger the dose of steroids. **GET PEOPLE OFF STEROIDS**. They cause hypertension, diabetes, avascular necrosis, and osteopenia. Only use them in flares.

- Life threatening cerebritis or nephritis can be treated with **IV Cyclophosphamide**.
- When the acute phase is past, **mycophenolate mofetil orally** can be used to continue treatment.
- Much like in RA, **NSAIDs** are saved for the end. Why? Because they treat symptoms - not the disease.
- Never use NSAIDs as monotherapy.

Treatment	*When*
Hydroxychloroquine	Everyone
Steroids	Flares only
IV Cyclophosphamide	Life-threatening illness Cerebritis, Nephritis
Mycophenolate Mofetil	Oral Cyclophosphamide Use after IV
Methotrexate	2nd line to Hydroxychloroquine
NSAIDs	Symptom control only
Azathioprine	Adjunctive
Biologics	Maybe, not yet approved

Drug-Induced Lupus

- There are a lot of drugs with a side effect profile of lupus.
- The ones you should recognize for the test (even if not prescribed all that often) are **hydralazine, procainamide, isoniazid**, and **alpha-methyldopa**.
- Drug-induced lupus presents with **skin and joint** symptoms (rash and joint pain), but will **spare the visceral organs**. It doesn't kill you - it just hurts and is annoying.
- Diagnose with **anti-histone antibodies** and stop the drug to reverse the disorder.

Lupus Nephritis

- This condition can be life threatening.
- Screen using **U/A and Umicro**, specifically screening for hematuria, casts, and proteinuria.
- If a diagnosis is necessary this is one of the few times where a **kidney biopsy** is the right answer.
- Treatment is with **IV cyclophosphamide** followed by scaling back to **PO Mycophenolate Mofetil.**

MONOARTICULOPATHIES

- When someone comes in with a **single hot joint** with a several **hours duration** (acute) there are a few possibilities.
- It's likely either a **septic joint** caused by an infection or a **crystal deposition** disease.
- To determine the diagnosis the history with **risk factors** becomes vital.
- But no matter how clear the story is, you can't miss a septic joint so always do an **arthrocentesis.**

1) Septic Arthritis

- A septic joint gets infected two ways: **direct inoculation** by trauma or by **hematogenous spread**.
- It really comes down to: Is it Staph aureus / Nongonococcal or is it Gonococcal? Staph can get in via **trauma** (hard to miss the arrow sticking out of the knee) or by hematogenous spread (think **IVDA / Endocarditis** septic emboli).
- Gonococcus gets in by **hematogenous spread only**, so look for the young sexually active adult with a **urethral discharge** and a couple of **days** of **constitutional symptoms** who now has a **hot, swollen knee**.
- Tapping the joint will show many **polys** (>50 WBC **90% Poly**).
- Start empiric antibiotics, then alter them as the stain, cultures, and sensitivities become available.

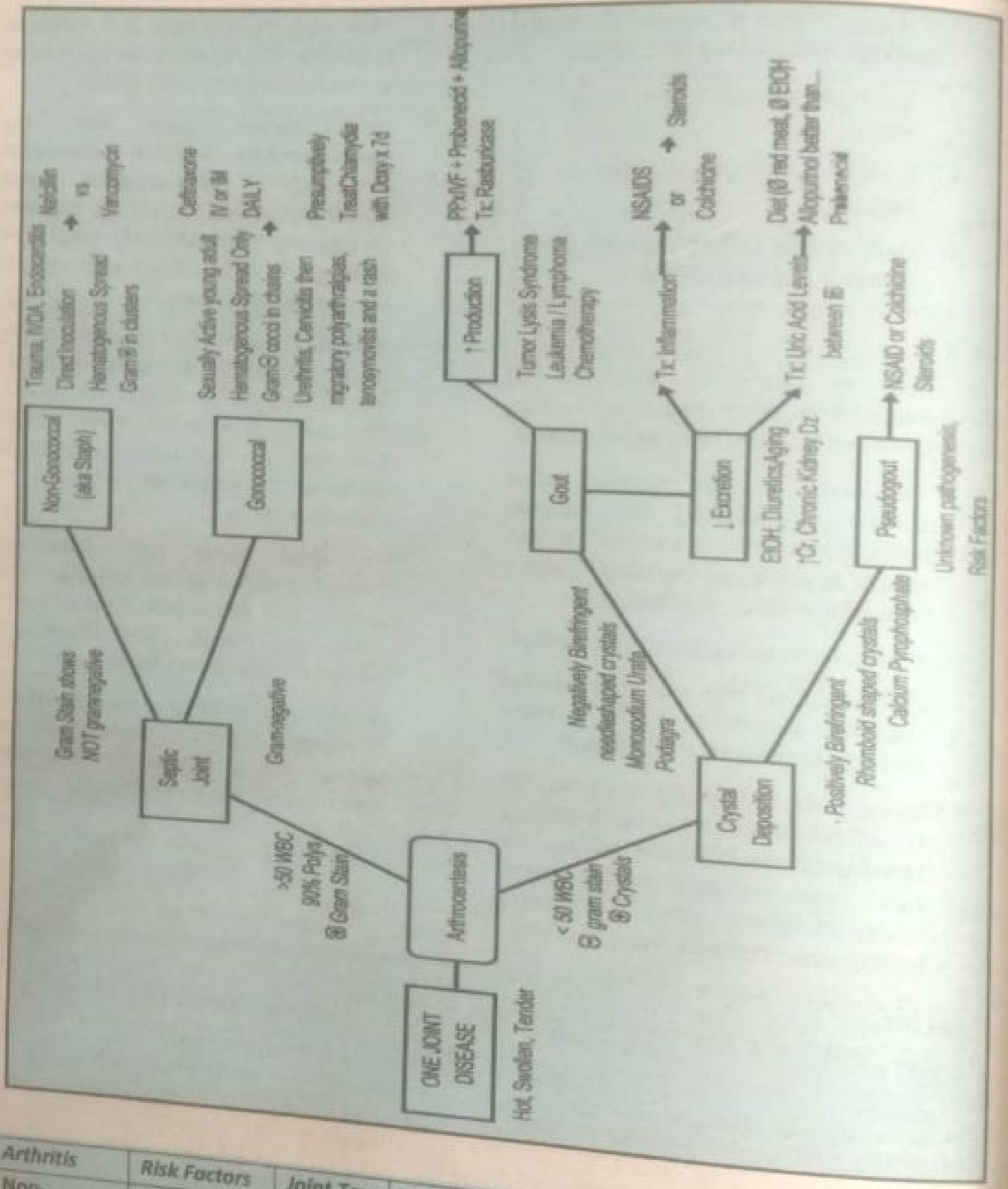
- If the gram stain is ***negative*** do **double coverage** (ceftriaxone + vancomycin).

> - *You're going to tap the joint either way.*
> - *You'll treat empirically based on risk factors.*
> - *You'll treat for BOTH if you don't get a definitive diagnosis on Tap.*

2) Gout

- Gout is caused by deposition of **monosodium urate crystals** in the joint space and exacerbated by **hyperuricemia**.
- Too much uric acid happens either because of **increased cell turnover** (production of uric acid secondary to DNA lysis) or by **decreased excretion** (usually a result of decreasing renal function).
- It's usually caused by decreased excretion.
- Look for the **old man** who drinks **alcohol** and is on a **diuretic** (all of these decrease the excretion capacity of the kidney).
- During an acute flare diagnose gout with an **arthrocentesis**; it'll show **negatively birefringent needle-shaped** crystals. The joint is exquisitely tender so a clear clinical history is sufficient - especially if **podagra** (inflammation of the great toe) is present.
- ***Treat acute gouty attacks*** with **NSAIDs** or **Colchicine**. Colchicine causes diarrhea so is dose limited by that side effect.
- ***Treat chronic gout*** with the **xanthineoxidase inhibitor allopurinol** (preferred) or the **uricosuric agent probenecid** to keep the uric acid between <6. Starting treatment may induce an acute gouty attack. Don't stop chronic therapy during this flare.
- Gout can get so bad that renal failure may result. This occurs during ***severe bouts*** that increase the production of uric acid. One such example is **Tumor Lysis Syndrome** (where a bulky tumor as in **Leukemia** or **Lymphoma** is blasted by **Chemotherapy**).
- *To avoid Tumor Lysis Syndrome*, prophylaxis with **vigorous hydration** and pretreat with **Allopurinol**. If the uric acid levels have already risen, lessen the burden of uric acid with **Rasburicase.**
- If the arthrocentesis shows **positively birefringent crystals**, it's **pseudogout.** The pathogenesis is unknown but it can be treated with NSAIDs and Steroids.

ACUTE		
NSAIDs	↓ inflammation	1st Line, Gastritis, CKD
Colchicine	↓ inflammation	2nd line, Diarrhea
Steroids	↓ inflammation	Last Line
CHRONIC		
Allopurinol	Xanthine-Oxidase Inhibitor	Maintenance, can cause acute flare
Probenecid	Uricosurics	Maintenance, can cause Uric Acid Stones


ONE JOINT DISEASE
Hot, Swollen, Tender
Arthrocentesis
>50 WBC
90% Polys
⊕ Gram Stain
< 50 WBC
⊖ gram stain
⊕ Crystals
Septic Joint
Gram Stain shows NOT gramnegative
Gramnegative
Non-Gonococcal (aka Staph)
Trauma, IVDA, Endocarditis
Direct Inoculation
Hematogenous Spread
Gram ⊕ in clusters
Nafcillin vs Vancomycin
Gonococcal
Sexually Active young adult
Hematogenous Spread Only
Gram ⊖ cocci in chains
Urethritis, Cervicitis then migratory polyarthralgias, tenosynovitis and a rash
Ceftriaxone IV or IM DAILY
Presumptively Treat Chlamydia with Doxy x 7d
Crystal Deposition
Negatively Birefringent needleshaped crystals
Monosodium Urate
Podagra
Gout
↑ Production
Tumor Lysis Syndrome
Leukemia / Lymphoma
Chemotherapy
PPx/MF + Probenecid + Allopurinol
Tx: Rasburicase
↓ Excretion
EtOH, Diuretics/Aging
↑Cr, Chronic Kidney Dz
Tx: Inflammation
NSAIDS or Colchicine
Steroids
Tx: Uric Acid Levels between
Diet (Ø red meat, Ø EtOH)
Allopurinol better than...
Probenecid
Positively Birefringent
Rhomboid shaped crystals
Calcium Pyrophosphate
Pseudogout
Unknown pathogenesis,
Risk Factors
NSAID or Colchicine
Steroids

Arthritis	Risk Factors	Joint Tap	Gram Stain	Culture	Crystals	Treatment
Non-Gonococcal Staph Aureus	IVDA, Endocarditis, Direct Trauma, Sepsis	>75 WBC 90% Polys	Gram ⊕Cocci in clusters	Staph	∅	Nafcillin or Vancomycin

Gonococcal	Unprotected Sex, Urethritis, Discharge, Ø Trauma	>75 WBC 90% Polys	Gram ⊖ Cocci in chains	Gonococcus	∅	Daily IV or IM Ceftriaxone
Gout	↑ Levels of uric acid old man on EtoH + Diuretics, Podagra	5-50	∅	∅	Urate Crystals negatively birefringent Needle Shaped	NSAIDs or Colchicine Steroids Allopurinol maintenance Probenecid maintenance
Pseudogout	↑ Calcium Pathogenesis Unknown	5-50	∅	∅	Pyrophosphate Crystals Positively Birefringent Rhomboid Shaped	NSAIDs or Colchicine Steroids

OTHER CONNECTIVE TISSUE DZ

Scleroderma

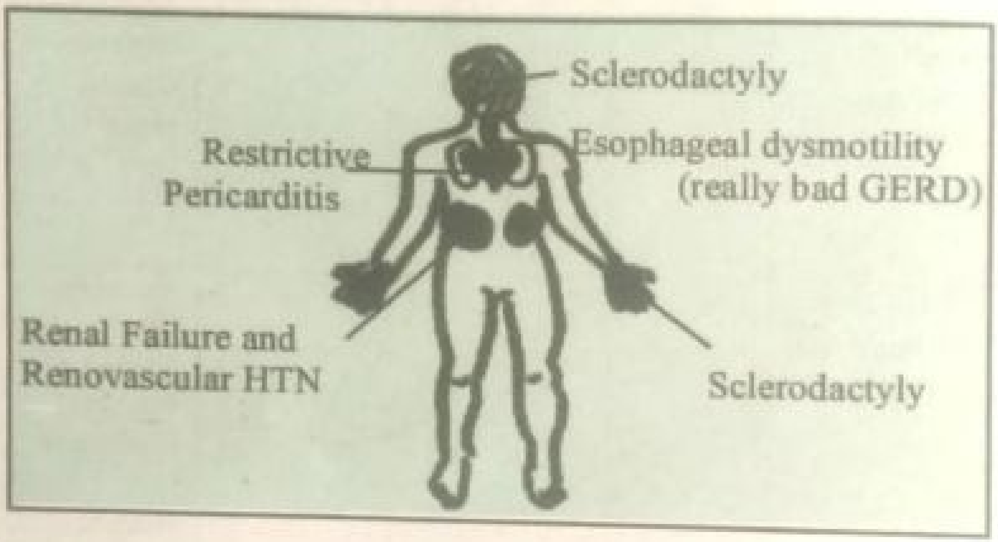
- Scleroderma is an **autoimmune disease** resulting in:

  1) **collagen** replacing **smooth muscle** and

  2) wide-spread extraneous **collagen deposition.**

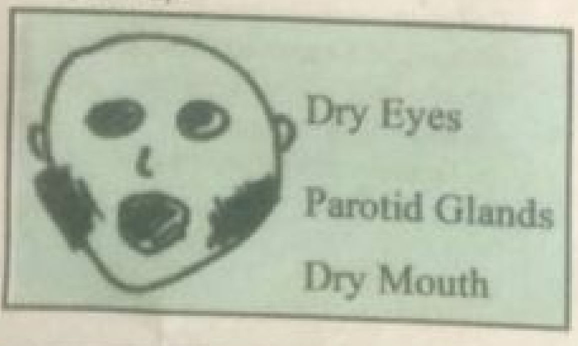
- The typical patient has **skin tightness** in the hands and face and may suffer some GERD or Raynaud's.
- In reality, there are **two types of scleroderma:**
  - *CREST* (**CREST** is a limited disease that **spares the heart and kidneys** but has **Skin and GI effects**).
  - *Systemic Sclerosis.* (**Systemic sclerosis** is a diffuse disease affecting the trunk with **cardiac** (restrictive cardiomyopathy) and **Renal** (renovascular hypertension) effects.).
- Scleroderma is mainly a clinical diagnosis but antibodies may aid getting there.
- **Anti-Scl-70** (topoisomerase I) is positive in systemic disease while **anti-centromere** is positive in CREST.
- There's also **no treatment** for the disease itself.
- Instead, treat the symptoms.
- Use **Calcium Channel Blockers** for **Raynaud's**, **Penicillamine** for **skin changes**, **steroids** for **acute flares**, and aggressive treatment of hypertension with **ACE-inhibitors.**
- Collagen in the renal arterioles prevents dilation and constrict. This creates a pre-renal picture by activating the renin-angiotensin-aldosterone axis, which exacerbates the hypertension.

CREST	Systemic Sclerosis
Calcinosis	CREST +
Raynaud's	Renal
Esophageal Dysmotility	Heart
Sclerodactyly	
Telangiectasia	
Anti-Centromere	Anti-Scl-70
PAH	ILD


Sclerodactyly
Restrictive Pericarditis
Esophageal dysmotility (really bad GERD)
Renal Failure and Renovascular HTN
Sclerodactyly

Sjogren's syndrome

- An inflammatory condition of **exocrine glands** due to **lymphoplasmacytic infiltration.**
- It can exist on its own (primary) or be part of another Rheumatologic disorder (secondary).
- It's easy to spot: **Dry Eyes** (Keratoconjunctivitis), **Dry Mouth** (Xerostomia), and **bilateral parotid enlargement**.
- It's a clinical diagnosis assisted by antibodies (**Ro** or **La** which are specific but not sensitive) and **tear production testing** (Schirmer test). There's **no treatment** so focus on **symptom control** (artificial tears / saliva).


Dry Eyes
Parotid Glands
Dry Mouth

Polymyositis / Dermatomyositis / Inclusion Body Myositis

- These three **inflammatory myopathies** are lumped together because their presentation, diagnosis, and treatment are all the same (well, except IBM, which has no treatment).
- The underlying pathogenesis (**T cell / Immune Complex / T cell** respectively) results in the presentation of **painful proximal muscle weakness** (difficulty in rising out of a chair but intact grip strength) occurring slowly over time. There may be systemic involvement.
- The way it comes to light is usually the **dermatologic signs**:

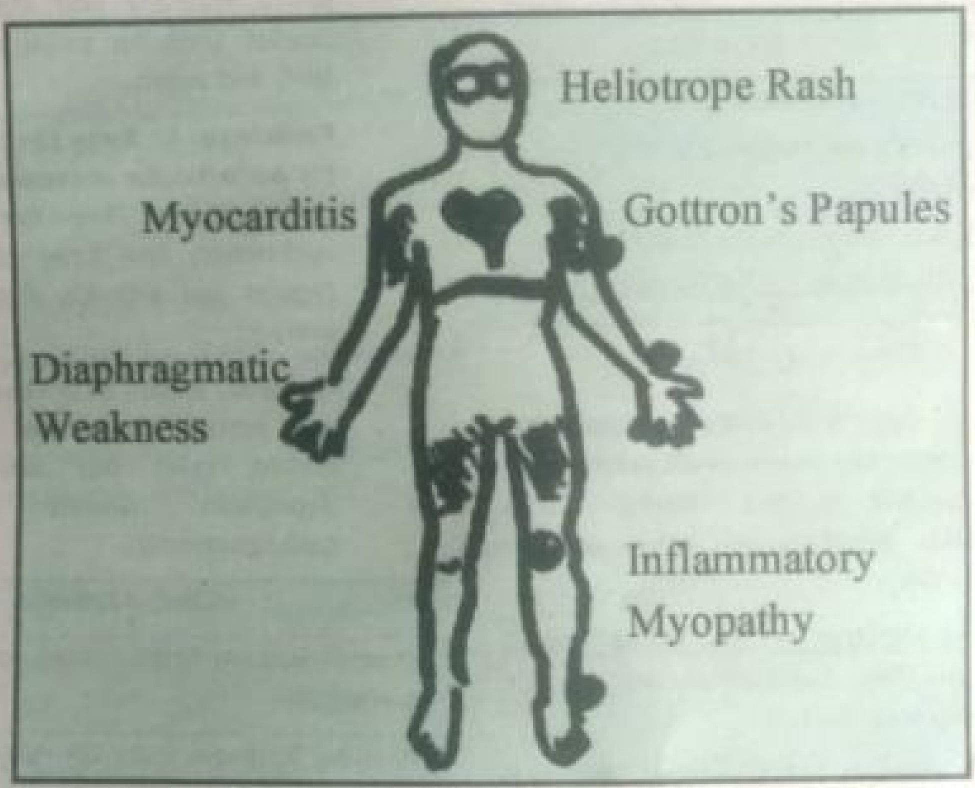
  1) erythematous rash on sun-exposed areas (**photosensitivity**),

  2) **Heliotrope rash**, a purple discoloration around the eyes with periorbital edema, and

  3) **Gottron's Papules** (pathognomonic), which are scaly areas symmetrically over

major joints (wrists, elbows, knees, ankles).

- The first test is always **EMG** to determine if it's a nerve conduction issue (MS, for example) versus muscular damage.
- A **muscle biopsy** is done to definitively diagnose and separates one disease from the other. Other tests may help.
- The **CK** will be **elevated** (muscular damage) and **Anti-Jo** or **Anti-Mi** antibodies may be present.
- The goal is to **check for occult malignancy** (as these are often a paraneoplastic syndrome) and treatment is with **high-dose steroids**.



	Scleroderma	*Sjogran's*	*DM/PM/IBM*
Pt	Female, Thickened Skin on fingers, GERD, Reynaud's	Female Dry eyes Dry mouth Bl Parotitis	Proximal Muscle weakness, tender, Heliotrope rash, Gottron's Papules F: DM +PM, M: IBM
Ab	Scl-70 = Diffuse Centromere = CREST	Ro	Jo
Dx	-	Schirmer Tear Production	EMG Bx MRI / CT (Cancer)
Tx	Penicillamine CCB Steroids ACE	Symptom Relief	Check for Malignancy High Dose Steroids

RHEUMATOID ARTHRITIS

Introduction

- Rheumatoid Arthritis is an **autoimmune disorder.**
- The pathology is a result of **pannus formation** at the joint, which leads to erosions and bony destruction.
- We don't know why it happens, but we know how to spot it and what to do about it.

> BONUS POINTS: Felty's syndrome
>
> *Rheumatoid Arthritis + Neutropenia + Splenomegaly =* ***Felty's***
>
> *If you see RA + Splenomegaly think Neutropenia*
>
> *RA + Neutropenia think Splenomegaly*

Presentation

- Classically there'll be **Prolonged morning stiffness** affecting **many small joints** (3 or more, usually in the hands), that's **symmetric;** vignettes will often use an **older woman**.
- *"Morning Stiffness" + "The Spine"* might come up. The reaction is to go for Ankylosing Spondylitis.
- If it involves the lower back it's ank spond.
- If it involves the neck (C1, C2) it's RA.

> **BONUS POINTS: Cervical X-ray**
>
> - *If a patient with RA is going into surgery for any reason a cervical film should be done since rheumatoid arthritis affects the cervical spine and the cervical spine only.*
> - *Ø Spine Involvement except C1 + C2*

Diagnosis

- There are a number of clinical criteria available to diagnose rheumatoid arthritis. They're not all needed, but some common findings are almost always present on a vignette.
- The old "wait 6 weeks," is now out; RA can be diagnosed right off the bat.
- **Serology.** Either the **Rheumatoid Factor** (cheap, sensitive) or the **Anti-CCP** (expensive, specific) can be used. If either is positive it counts for serology.
- **Joints.** There must be **symmetric arthritis** that involves **more than three joints** and **spares the DIPs**. Both the number of joints involved and the symmetry are crucial. Look for small joints like hands, feet, and wrists.
- **Radiology.** An **X-ray** can be used to assess for **periarticular osteopenia** and **marginal bony erosions**. These findings will also be symmetric. The x-ray can also identify regular old arthritis if osteophytes are seen.
- **Nodules.** Biopsy of a Rheumatoid Nodule will reveal **cholesterol** deposits. This finding rules out another potential deposition disease. These are pathognomonic.

Clinical Criteria
Symmetrical Arthritis, often of the **hands, Sparing DIP**
Morning Stiffness for > 60 minutes, **improves** with use
Multiple Joint Involvement (**> 3**)
Radiographic Destruction of Joints (**erosions**)
+ Rheumatoid Factor or **+ Anti CCP**
Rheumatoid Nodules

> *Nobody Should Have Rheumatoid Symptoms* ***3*** *times* ***(X)***
>
> ***N****: Nodules*
>
> ***S****: Symmetric*
>
> ***H****: Hands*
>
> ***R****: RF or CCP*
>
> ***S****: Stiffness*
>
> ***3****: 3 or more joints*
>
> ***X****: X-ray findings of erosions*

Be Careful

In life, you can have Rheumatoid Arthritis with negative RF and negative Anti-CCP, or no Rheumatoid Arthritis with positive RF and positive Anti-CCP. On a test it's always black and white: if positive, then disease, if negative, then no disease.

NSAIDs + DMARDS + Biologics .... Steroids

(Sxs) (everyone) (severe) (flares)

Treatment

- Get these patients on disease modifying agents as soon as possible.
- Start the treatment of RA with DMARDs as soon as possible.
- **Methotrexate** is **first line** for RA.
- Leflunomide can be used if methotrexate can't be.
- Hydroxychloroquine and Sulfasalazine have long-acting effects that may be used together with methotrexate to avoid biologic therapy (doubling up is ok).
- **Hydroxychloroquine** is also appropriate for **non-erosive** mild disease and **during pregnancy**.
- The goal is treat-to-target (disease remission).
- If DMARDs fail **add biologics**. Before starting biologics a **TB screen** and **vaccines** must be given as they significantly compromise immune function.
- **Corticosteroids** should be **avoided** - *except during life threatening flares* – to reduce long-term systemic side effects.
- **NSAIDs** can be used to control symptoms and are adjunctive therapy. **NEVER use NSAID MONOTHERAPY.**

Treatment

DMARD	Methotrexate (1st line) Leflunomide (2nd line) Hydroxychloroquine (pregnancy) Sulfasalazine (additive
Anti-TNF	Etanercept Infliximab Rituximab
Glucocorticoid	Flares, get off this as soon as possible
NSAIDs	Supplemental only, NEVER MONOTHERAPY

SPONDYLOARTHROPATHIES

Introduction

- This group of diseases are unique in that they show a predilection for the **spine**, particularly the **sacroiliac joints**, and have a higher incidence in **men** (much unlike the majority of rheumatologic diseases).
- There's a correlation to **HLA-B27** but it isn't useful for diagnosis.
- These patients are **seronegative**, they have no RF, CCP, or ANA reactive antibodies.
- What separates them from each other is their **extra-articular involvement** and links to other **inflammatory conditions**.

HLA-B27 doesn't help - DON'T order it.

UNLESS you have a clear diagnosis of ankylosing spondylitis despite negative films (x-ray and MRI)

RF, CCP, ANA don't help - DON'T order them.

1) Ankylosing Spondylitis

- Ankylosing spondylitis is the most commonly tested seronegative arthropathy.
- It occurs in men in their **20s** and **30s**.
- They will have **lower back pain** with **morning stiffness** that improves with use.
- It's caused by **sacroiliitis** with **fusion of the sacral joints** and calcification of tendons, which produces the **bamboo spine** on X-ray. Other tendons can calcify as well - especially the **Achilles tendon**.
- It can be associated with inflammatory bowel disease (distracting towards enteropathic) but its course is different.
- The treatment is based on severity and presence of axial vs peripheral joint involvement.
- Therapy generally starts with **NSAIDs**, escalates to **Methotrexate**, and if all else fails moves to monoclonal antibodies (TNF-alpha inhibitors) like **Etanercept**.

32 year old man with lumbar stiffness in the morning who gets an x-ray showing 'any positive finding' of the lumbar spine. The vignette should NOT include something about diarrhea.

Start him on NSAIDs and escalate to Methotrexate. Monoclonal antibodies CAN be used to treat the pain (unlike all other seronegatives).

TNF-Alpha-Inhibitors

- *Etanercept*
- *Infliximab*
- *Adalimumab*

2) Reactive Arthritis

- People with HLA-B27 who also get **nongonococcal urethritis** (usually Chlamydia) will "react" and develop an **asymmetric bilateral arthritis** of the **lower back** and **hands** as well as a **conjunctivitis**.
- Treating the underlying infection will prevent this **acute** disease from transforming into chronic.
- Treat the Chlamydia with **doxycycline** and arthritis with **NSAIDs**.

Gonococcal Urethritis = Septic Arthritis (one joint)

Non-Gonococcal Urethritis + Arthritis = Reactive Arthritis (back and hands)

Urethritis + Arthritis + Uveitis = Reiter's Syndrome

3) Psoriatic Arthritis

- Psoriasis + Arthritis is psoriatic arthritis.
- The main joint involved will be in the **hands**.
- It's a **symmetric PIP** and **DIP arthritis** with **erosive pitting** of the nails.
- The arthritis may precede the psoriatic plaques (making the diagnosis difficult).
- The goal is symptom control with **NSAIDs** if there's mild arthritis and NO skin disease.
- Use **Methotrexate** if it's severe or there are skin findings, **Anti-TNF** if Methotrexate resistant.

NSAIDs: Mild arthritis and no / 'meh' skin findings Methotrexate: Severe arthritis and real skin findings TNF-a Inhibitors: Nonresponsive to Methotrexate

~~Steroids~~: no... Steroids bad and lead to flare of psoriasis

4) Enteropathic / IBD-Associated

- While ankylosing spondylitis is associated with, but independent of IBD's course, this disease directly correlates with IBD.
- Treating the IBD fixes the arthritis.
- The arthritis is **symmetric** and **bilateral, non-deforming, peripheral** (fingers), and **migratory**.
- It also involves the lower back.
- The person will have some history of diarrhea to tell you they have IBD.

> *See how this is different from Ankylosing Spondylitis? Treating IBD makes this better. Treating IBS in AS does not.*

Disease	*Presentation*	*Diagnosis*	*Extraarticular*	*Treatment*
Ankylosing Spondylitis	Back Pain + Morning Stiffness relieved by exercise (Sacroiliitis)	Bamboo spine on X-ray	IBD but independent of IBD course	NSAIDs Steroids Anti-TNF
Reactive Arthritis	Nongonococcal Urethritis Conjunctivitis Asymmetric Bilateral Arthritis	∅ PCR/DNA Chlamydia	Nongonococcal Urethritis (usually Chlamydia	Doxycycline and NSAIDs
Psoriatic Arthritis	Psoriatic Patches Erosive pitting of nails MCP, DIP, PIP Arthritis	∅	Psoriasis Arthritis may appear First	UV light NSAID (no skin) Methotrexate (skin)
Enteropathic	Non-deforming, migratory, symmetric Bilateral Arthritis In a patient with IBD	∅	IBD and dependent of IBD course	Tx IBD with ASA compounds (mesalamine)

VASCULITIS

- Vasculitis are a bit peculiar.
- They're often a diagnosis of exclusion as they're considered only after other diseases have been ruled out.
- Let's focus on the few test associations for classic presentations.

LARGE VESSEL VASCULITIS

Giant Cell Arteritis

- Also called **temporal arteritis,** this is the **most common** primary vasculitis.
- It effects the arteries of the external carotid (the temporal artery and ophthalmologic artery).
- The classic presentation is **age > 50** person with **unilateral temporal headache** and a **tender swollen temporal artery**.
- Another pattern could be visual changes or jaw claudication.
- This is an intensely inflammatory disorder, so **systemic symptoms** may be present (elevated ESR, weight loss, low-grade fever, and malaise).
- **GIVE STEROIDS FIRST**
- Even though the diagnosis is definitely made with a **biopsy**, the risk for blindness is too great; treatment should precede the diagnostic step.

Polymyalgia Rheumatica

- While this is actually **not a vasculitis** it's so commonly associated with Giant Cell Arteritis that it's discussed here.
- PMR presents with **symmetric pain and stiffness** in the **shoulder, neck,** and **hips**.
- It'll present as a proximal muscle weakness similar in pattern to the idiopathic inflammatory myopathies but with a **normal CK** (the ESR and systemic signs of inflammation are present).
- This disease requires no diagnostic step, though an angiogram could rule out other diseases. It responds well to **steroids**.

Takayasu Arteritis

- This disease is super rare and has the same pathology as GCA, but instead of the distal arteries it impacts the vessels of the **aorta** and its major branches (subclavian, renal, femoral).
- There are systemic signs (↑ESR, weight loss, fever), but what you're keying in on is the **absent pulses in large vessels** (brachial, femora, carotid).
- Look for a **young person** (< 40 years old) who has **systemic inflammation** and large vessel impairment.
- An **angiogram** will make the diagnosis.
- Treat with **high dose prednisone**

SMALL VESSEL – ANCA RELATED

Granulomatosis with Polyangiitis (Wegner's)

- Most common ANCA associated vasculitis.
- GPA is usually **c-ANCA positive**.
- Look for **renal + lung + nasal**.
- This is usually seen on the test as **hematuria and hemoptysis** but **also with nasal involvement**.
- A biopsy of affected tissue is required for treatment; it will show vasculitis and necrotizing granulomas.
- Treatment is aggressive: **steroids and cyclophosphamide**.
- Other DMARDs can be used as maintenance therapy.

MEDIUM VESSEL VASCULITIS

Polyarteritis Nodosa

- PAN is associated with **Hepatitis B** but can exist on its own.
- It's tough to diagnose because it affects so many organs.
- When **vasculitis in multiple organs** at the same time **without a common vascular distribution** is seen, think PAN.
- In the kidneys it causes a non-glomuerlonephritis vasculitis (**renal failure**).
- In the gut is causes mesenteriC vasculitis (**mesenteric ischemia**).
- In the nervous system it causes an asymmetric painful motor and sensory neuropathy (**mononeuritis multiplex**).
- In the skin it causes **purpura** and **painful nodules**.
- What will probably happen is that you will go hunting for ONE problem and do some vascular imaging like an **angiogram**. T
- hat angiogram will reveal **aneurysms** and **stenosis** in medium sized vessels. Treatment is aggressive.
- Start with **high-dose** steroids and **cyclophosphamide**.
- Treat Hep B.

Kawasaki Disease

- This is as **Asian Childhood** Disease (look for infants and children, most commonly Asian boys).
- The buzz phrase is strawberry-like **tongue**. A
- lso look for the **truncal rash** with a palmar **and plantar** erythema with **desquamation**.

- This can cause vasculitis of the coronary arteries leading to myocardial infarction in a child.
- Treatment is with **IVIG** and **Aspirin** (even though you're not supposed to give kids aspirin).

SMALL VESSEL – COMPLEX MEDIATED

Cryoglobulinemia

- Think of cryoglobulinemia when there's **palpable purpura** and **Hepatitis C**.
- Assess for **cryoglobulins** in the serum.
- Other clues may be a positive RF, elevated ESR, and **decreased compliment**.
- Treatment can be with **steroids**, cyclophosphamide, rituximab, and **plasmapheresis** (in increasing order of severity).

Henoch–Schönlein purpura

- HSP is suspected when there's **palpable purpura** and **abdominal pain** or **abdominal bleeding**.
- The kidneys can be involved.
- The diagnosis is made by **biopsying** the effected tissue (usually the skin) to reveal a **leukocytoclastic vasculitis**.
- For treatment, **steroids** are the main option.

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